Chemistry of 3,4-furandiylbis[trimethylsilanes]

(3,4-bis(trimethylsilyl)furans)

by

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Contents

Page

I. Acknowledgements

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June, 1989

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II. Abstract

3,4-Bis(trimethylsilyl)furan (34) and 2-methyl-3,4-bis(trimethylsilyl)-furan (35) have been synthesized. Compound 34 was found to undergo Diels-Alder reaction with dienophiles, though less reactive, and extrusion of bis(trimethylsilyl)acetylene occurred when treated with acetylenic dienophiles.

Both 34 and 35 were found to undergo regiospecific electrophilic substitution at the unsubstituted α-position and gave a pair of regio-isomers. In addition, 2-benzoyl-3-trimethylsilylfuran (36), 2-benzoly-4-trimethylsilylfuran (37) and 2-benzoly-5-methyl-3-trimethylsilylfuran (38) were found to undergo regiospecific deuteriodesilylation.

III. Introduction

The furan nucleus represents the main structural features both of several natural products (farnesane furans, furanoid fatty acids and marine products, eremophilane, butenolides), and of some useful key-intermediates.

The majority of the naturally occurring compounds containing a fully unsaturated furan ring are terpenoid in character. Furans which occur in nature in a reduced or otherwise modified form include pentose sugars such as ribose and deoxyribose, which are components of nucleic acids. From a chemical perspective, it is thus clear that the syntheses of polysubstituted furans seem especially worthy of study.

Furthermore in our continuation of the study of the Diels-Alder reaction between furans and strained alkynes, we are interested in preparing effective precursors for the synthesis of substituted furans.

In order to provide a frame work of reference for the discussions to be presented in the later Sections of this Thesis, a brief review of the reactions of the furans is given below.

III.1 Reactions of furan

A. Electrophilic Substitutions

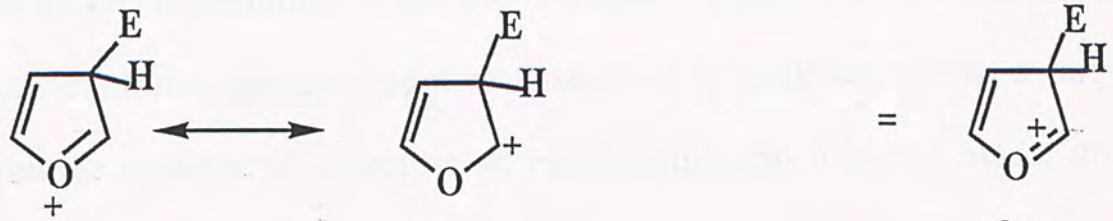
Electrophilic substitutions are the most characteristic reactions of the electron-rich furan ring. Furan can be allylated[1], benzylated[2], acetylated[3] or alkylated[1] in the C-2 position. Generally, electrophilic attack at the 3(4)-position is negligible unless both 2(5) position are filled or unless it is otherwise forced, as in a cyclization reaction[4]. Probably very small amounts of

3(4)-substitution occur and are overlooked in ordinary work though they can be found if sought carefully. Ciranni and Clementi[5] have studied the α/β ratio in detail. Thus, acylation of furan with acetic anhydride under various conditions produced α/β ratios between 800 and 6800 and required isotopic analysis (^{14}C) for the necessary precision[5].

In order to understand why electrophilic attack occurs more readily at the α-position than at the β-position, it is most easily explained in terms of resonance stabilization or delocalization of the positive charge in the intermediate cation. Scheme 1 shows the resonance structures of α- and β-addition of electrophile. It can be seen that resonance stabilization or delocalization of the positive charge is greater in the case of the cation **1**, derived from α- addition. In the cation **2**, derived by β-addition, the C4-C5 double bond is not and cannot be mesomerically involved in the delocalization of the positive charge.

Scheme 1

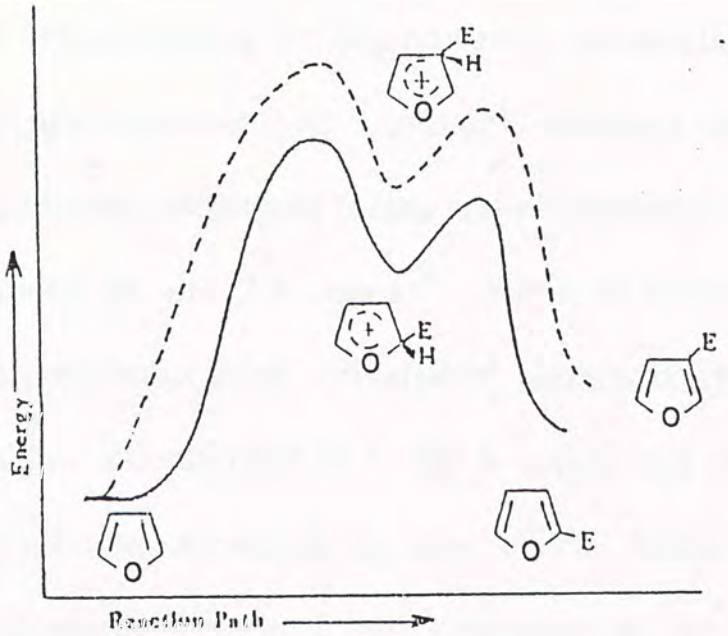
1



2

The energy profile for this type of reaction (Figure 1) also demonstrates that the σ- complex which is involved in α-substitution is stabilized to a greater extent than the one involved in β-substitution. In fact, most monoheteroatomic, π excessive, five membered aromatic rings undergo preferentially electrophilic substitution on the carbon α to the heteroatom.

Figure 1



Politzer et. al.[6] have computed the potential distribution for the furan molecule using a deorthogonalized CNDO/2 molecular wave function and found that the potential to be positive everywhere except the oxygen atom where it is negative. Still more striking is the fact that, when a hydrogen atom at any position was removed out of the plane into a tetrahedral positions, a negative potential was developed along the fourth tetrahedral bonds. This is the direction of approach by an electrophile. Since the C-2 and C-5 position are close to the oxygen atom the three adjacent negative areas tend to coalesce, giving a large negative volume capable of attracting an electrophile and it is this effect that might account for the selective substitution at the C-2(5) positions, for the

negative volumes near the 3(4)-position are small and isolated.

Empirical correlations can readily be made on the directing effect of the substituents from the large body of experimental data available[7], furans substituted in the C-2 position with a +I or a -I, +M substituent always undergoes electrophilic substitution at the C-5 position. For a -I, -M substituent at the C-2 position, the C-5 position will be deactivated by mesomeric effect, but this is generally overwhelmed by the powerful orientational effect of the heteroatom and 5-substitution ensued. Lewis acid enhances the -M effect of the substituent in 2-carbonyl substituted furans and electrophilic substitution gives appreciable amounts of the 2,4-isomer[8]. For a +I substituent at the C-3 position, the C-2 position is more activated by electronic effects, but the C-5 position is unhindered and mixtures of 2- and 5- substituted isomers are usually obtained. The proportions depend on the size of the 3-substituents and then nature of the electrophile. For a -I, +M substituent at the C-3 position, the effects of the heteroatom and the substituent are in alliance which will direct the electrophile to the C-5 position.

For disubstituted compounds the position of attack may be deduced from the directing effect of the heteroatom and the substituents. In some cases of 2,5-disubstituted compounds, replacement of a substituent such as a carbonyl group may occur in preference to attack at C-3 or C-4 position.

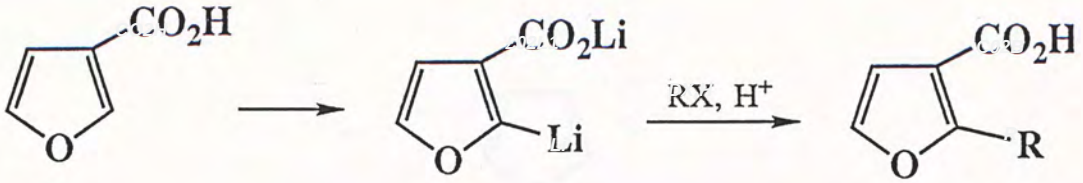
B. Nucleophilic reactions

Some furans bearing electron withdrawing substituents can undergo nucleophilic substitution; for example, lithium fluoride can convert

5-bromofuran-2-carboxaldehyde into 5-fluorofuran-2-carboxaldehyde. Azide and other nucleophiles can displace the nitro group in 5-nitrofuran-2-carboxaldehyde and some other typical examples have been discussed[9]. Although nucleophilic substitutions of halofurans have not been extensively studied, it is well known that 2-bromo and 2-chlorofuran can be displaced by piperidine[10]. In addition, neither 2-bromo nor 2-iodofuran reacts with sodium methoxide at 100°C[11], but 3-iodofuran can be transformed to 3-methoxyfuran upon treatment with sodium methoxide and cuprous oxide in methanol and will be converted to 3-cyanofuran with cuprous cyanide in quinoline[12].

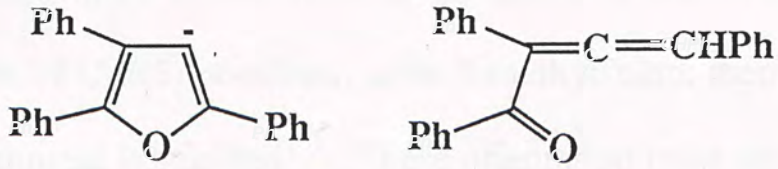
Furan and alkyl furans do not react with nucleophiles by addition or by substitution. The strong bases, however, can effect deprotonation at the α-position. In recent years, lithiated furans have become increasingly important in furan chemistry because they can be formed selectively and also react selectively in mild conditions, to give substitution products[13]. Furan is lithiated at the α-position by butyllithium and it can also be 2,5-dilithiated[14] or 2,5 dipotassiated[15] by careful control of reaction conditions. 3-Furyllithium can be prepared from 3-bromofuran by bromine-lithium exchange. However, butyllithium removes α-bromine in preference to β-bromine although it can still be removed subsequently. Considerable selectivity is also possible in the lithiation of substituted furans; for [illegible]a-3-carboxylic acid is converted by lithium diisopropylamide into the [illegible]io-furan-3-carboxylate (3) and hence can be selectively alkylated and [illegible]eriated at the C-2 position[16]. The alkylation and acylation of 3-lithiofu[illegible] have proved to be a synthetically

useful reaction[17]. It is because many naturally occurring furans are 3-alkyl and 3-acyl derivatives.



3

Very few furan 3-carbanions are stable except at low temperatures and ring opening is common. Pearson and Gilchrist[18] reported that the fate of the unusually stable carbanion 4 depends upon both solvent and temperature. At room temperature and in benzene, it partly opens to give the allenic ketone 5; in ether it is fairly stable. In hexane, the 3-lithiofuran is precipitated unless heated to 65°C when it isomerizes to acetylenic salts, giving the allenic ketone 5 with water.



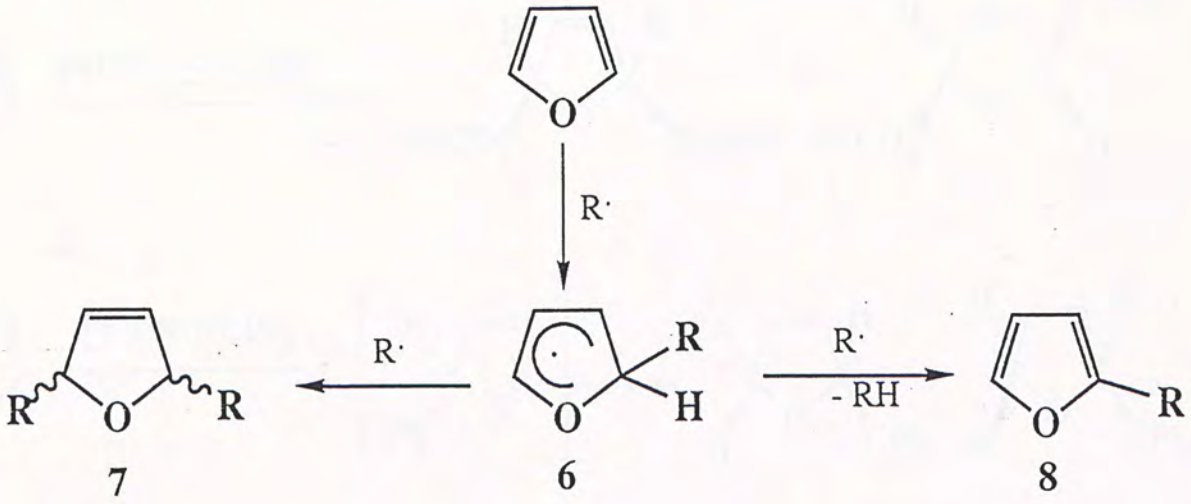
4 5

C. Radical reactions

Furan undergoes both substitution and addition with radicals. Radical attacks the furan nucleus firstly at the C-2 position yielding an intermediate radical 6 which then followed by another radical addition at the C-5 position leading to a 2,5-disubstituted dihydrofuran 7. It will also lose a hydrogen atom, thus leading to a 2-substituted furan 8 (Scheme 2). There are other possibilities,

such as radical dimerization, but the two reactions shown in Scheme 2 are the chief ones.

Scheme 2

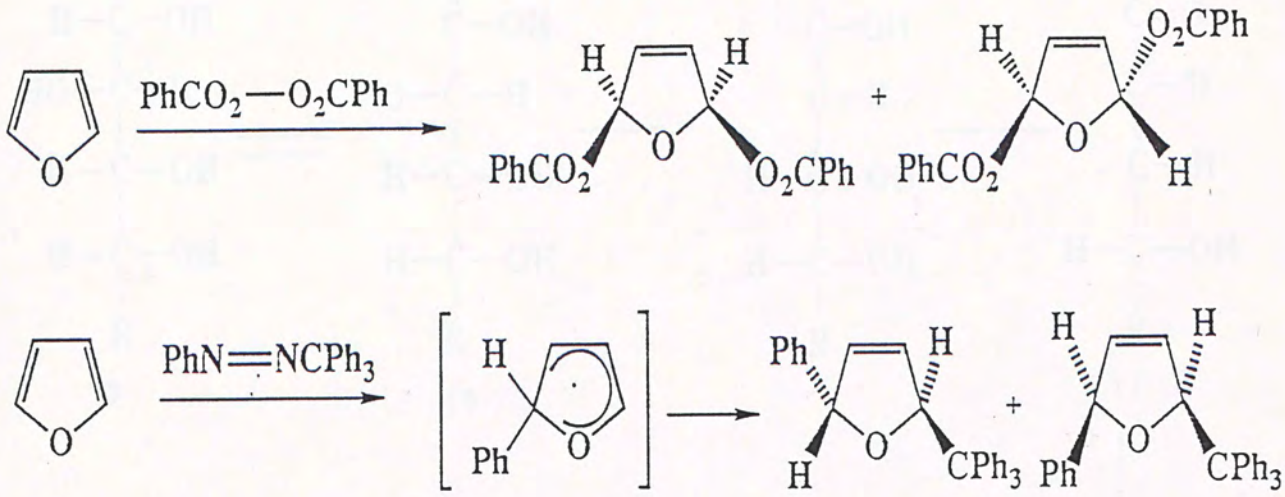


Methyl radical, generated from diacetyl peroxide, attacks 2-methylfuran at the C-5 position preferentially. If both C-2 and C-5 positions are occupied as in 2,5-dimethylfuran, there is still little or no attack at the C-3(4) position. If there is a choice of C-2(5) positions, as in 3-methylfuran, then that adjacent to the methyl substituent is selected[19]. These orientation rules are similar to those for electrophilic substitution (vide supra).

Both dibenzoyl peroxide[20] and phenylazotriphenylmethane[21] give addition products with furan (Scheme 3). In the case of phenylazotriphenylmethane, this has been attributed to the high steady-state concentration of the fairly stable triphenylmethyl radical. In the case of dibenzoyl peroxide, furan appears to capture benzoyloxy radicals before they lose carbon dioxide and yields the stereoisomeric 2,5-dibenzoates with almost no carbon dioxide evolution. 2,5-Dimethylfuran is also very reactive but undergoes attack at the methyl

groups and yields 5-methylfurfuryl benzoate. 2-Methylfuran exhibits intermediate behaviour and undergoes both types of attack[22].

Scheme 3

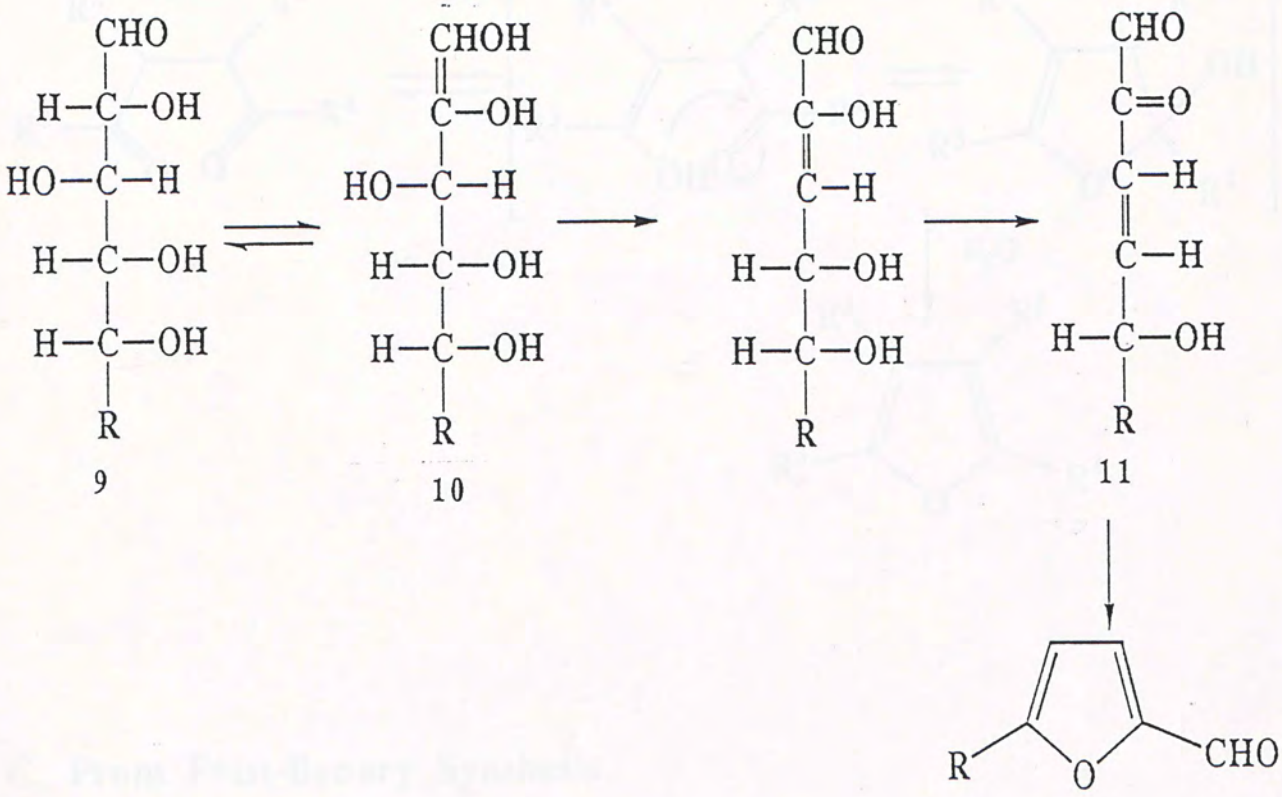


III.2 Synthesis of furan ring

A. From carbohydrate

It is well known that sugars can be converted into furan derivatives by acid treatment. These reactions have been studied by isotopic labelling techniques[23]. The aldose **9** or 2-ketose, is initially converted to 1,2-enediol **10** in a reversible reaction. The enediol **10** suffers consecutive dehydrations to give **11**, which then undergoes acid-catalysed cyclization (Scheme 4).

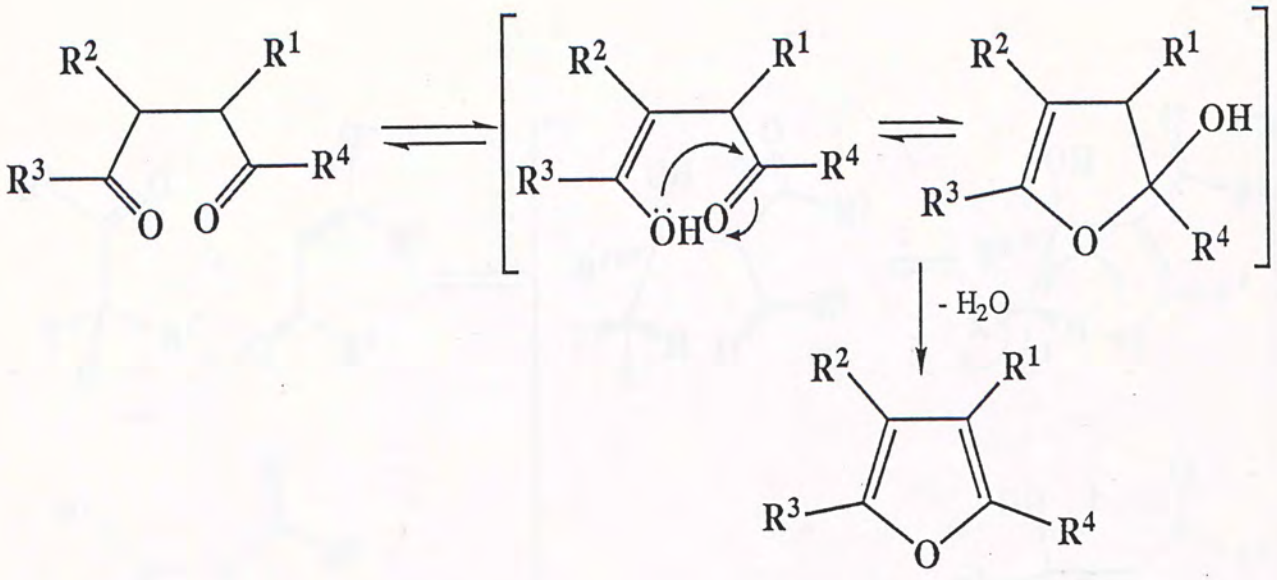
Scheme 4



B. From Paal-Knorr Synthesis

Acidic reagents can bring about the cyclization of 1,4-dicarbonyl compounds to the desired furan derivatives and the reaction generally proceeds in high yield. Usually, non-aqueous acidic conditions are empolyed to encourage the loss of water. The process may involve the oxygen of the enol form of one of the carbonyl groups adding to the carbon of the other carbonyl group. The process is completed by the elimination of water (Scheme 5).

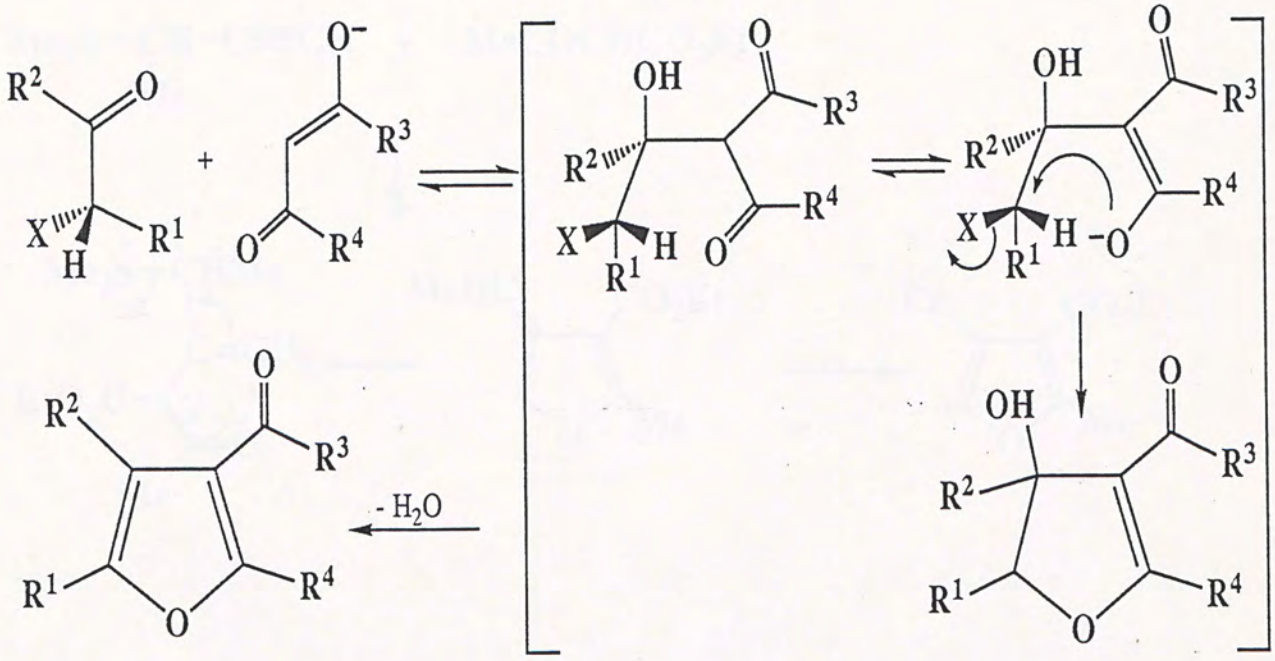
Scheme 5



C. From Feist-Benary Synthesis

Condensation of an α-halocarbonyl with a β-ketoester, usually carried out in the presence of aqueous base; provides a synthesis of furans bearing an ester substituent at the β-position. The reaction probably involves an aldol condensation with the carbonyl group of the α-halocarbonyl, followed by the formation of the oxygen ring by intramolecular displacement of halide, and finally loses water (Scheme 6). The reaction nearly always proceeds to produce an aromatic furan. However, 3-hydroxy-2,3-dihydrofurans have been isolated in certain cases[24]. Although by no mean a proof, the isolation of such compounds is a strong indication that the normal Feist-Benary synthesis proceeds via such a compound.

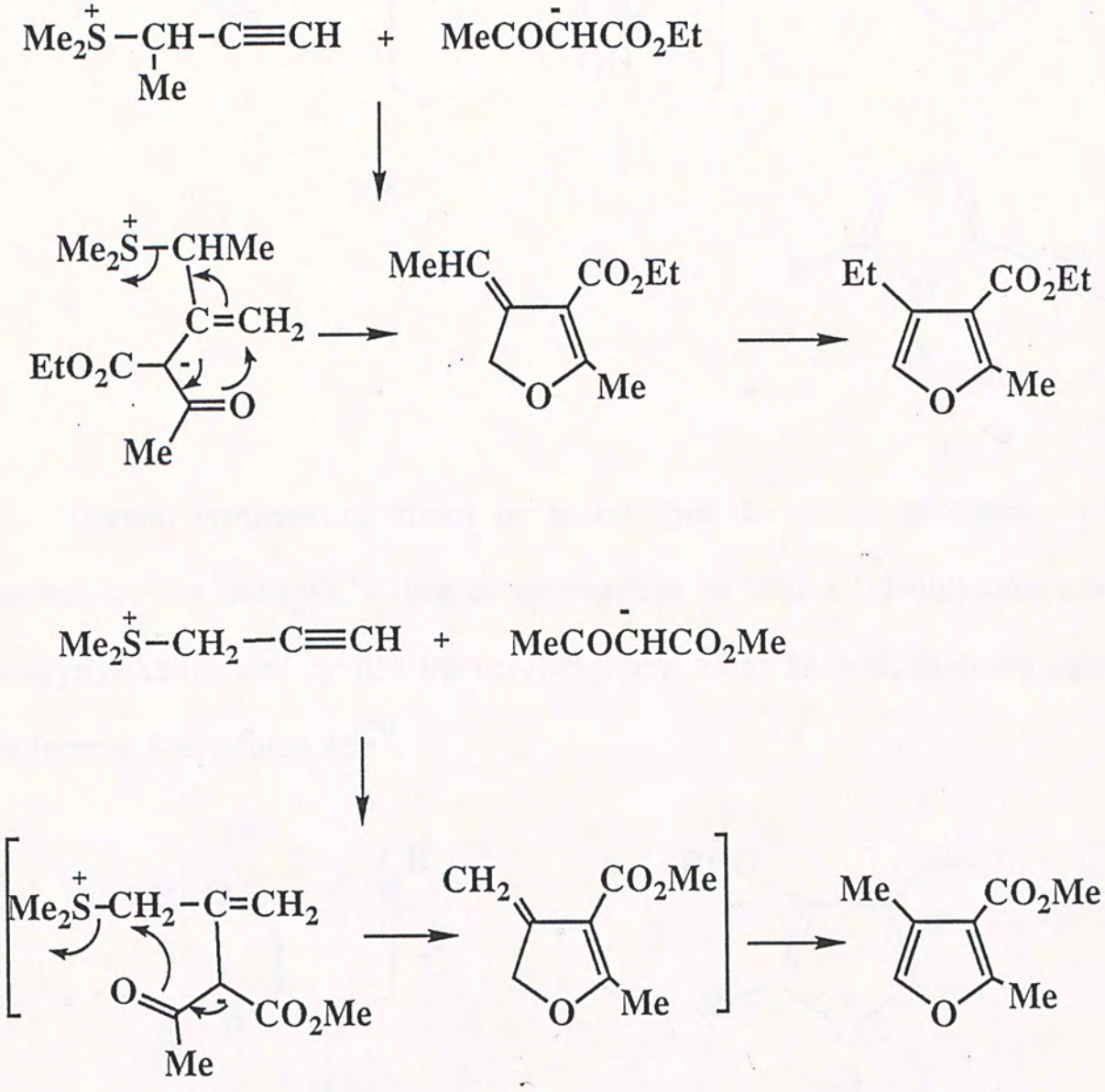
Scheme 6



D. From alkynes and cumulenes

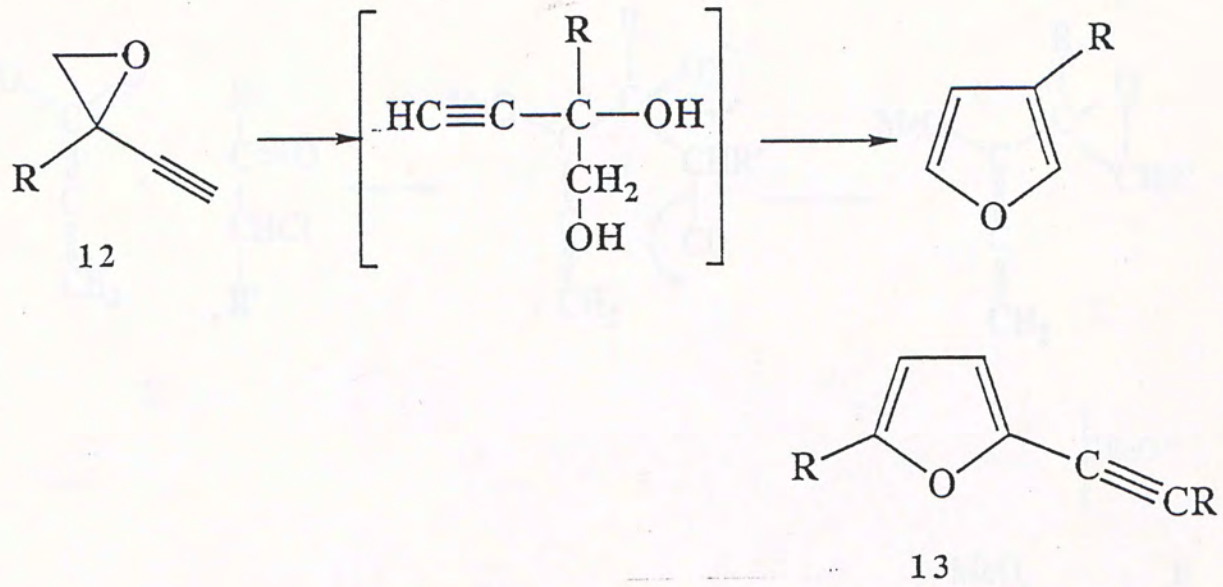
Since cumulenes and alkynes are often easily interconvertible and several of the alkyne-based syntheses may well proceed through allenic intermediates. Prop-2-ynyl sulfonium salts undergo prototropic rearrangement readily and the allenes formed are susceptible to nucleophilic addition by the enolate anions of 1,3-dicarbonyl compounds. The carbonyl oxygen attacks C-1 if this position is unsubstituted, but if C-1 is substituted then attack occurs at C-3. The cyclized products then afford furans by prototropic rearrangement[25] (Scheme 7).

Scheme 7



2-Alkyl-2-ethynyloxiranes **12** on treatment with aqueous acidic mercuric sulfate yields 3-alkylfurans. The reaction probably involves the glycols as intermediates and nucleophilic attack occurs at the terminal carbon atom (Scheme 8)[26]. Similarly, acetylenic glycols can also be efficiently cyclized to furans by mercuric chloride[27], or by bistriphenylphosphinepalladium salts, and diacetylenic glycols to yield acetylenic furans **13**[28].

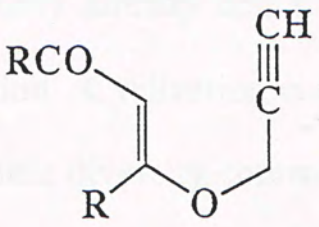
Scheme 8



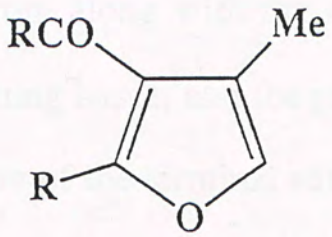
12

13

Several syntheses of furans are based upon the use of acetylenes to form carbon-carbon linkages, a simpler approach is to treat a 1,3-dicarbonyl with a propynyl halide and cyclize the resulting enol ether **14** with mercury catalysts to form a 3-acylfuran **15**[29].



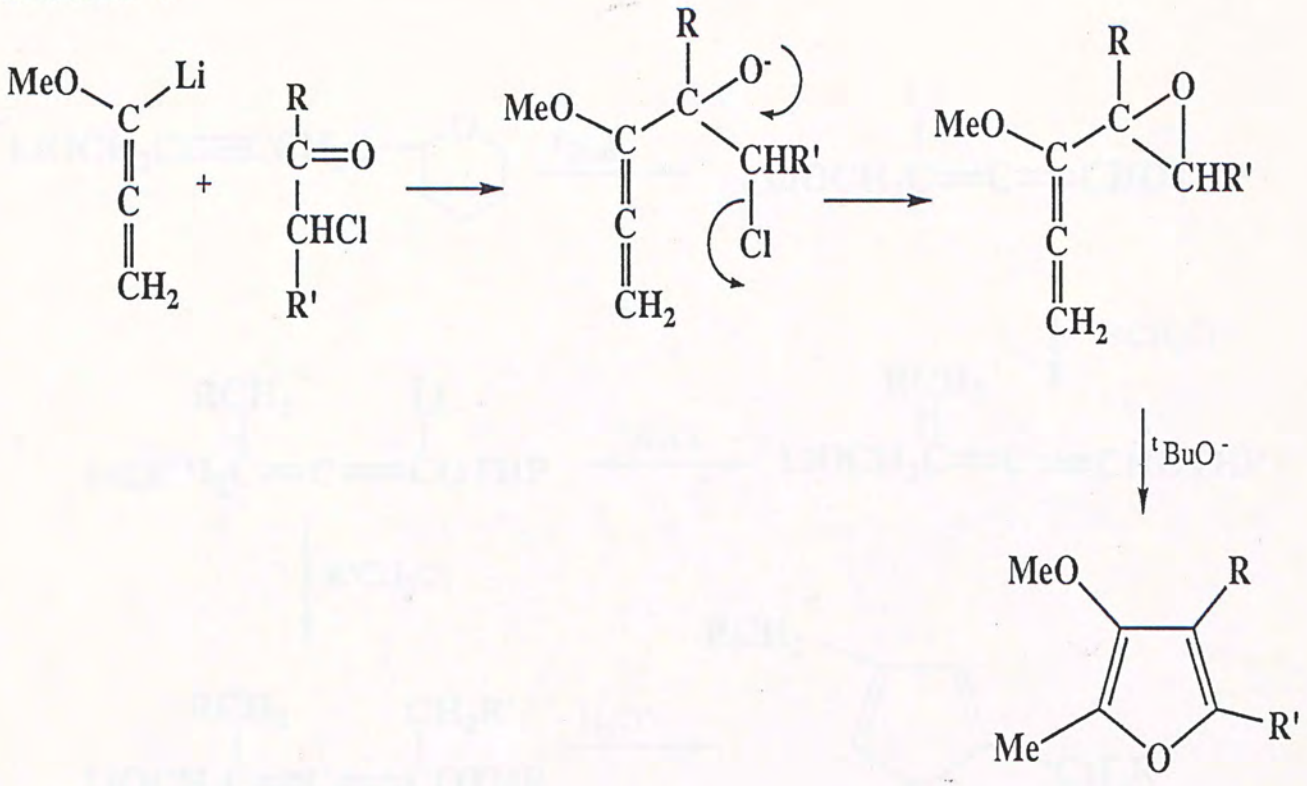
14



15

Methoxyallene is easily lithiated by butyllithium and is converted into an allenic epoxide that can be isomerized by tert-butoxide into a furan (Scheme 9). This method is particularly suitable for the preparation of 3-methoxyfuran derivatives[30].

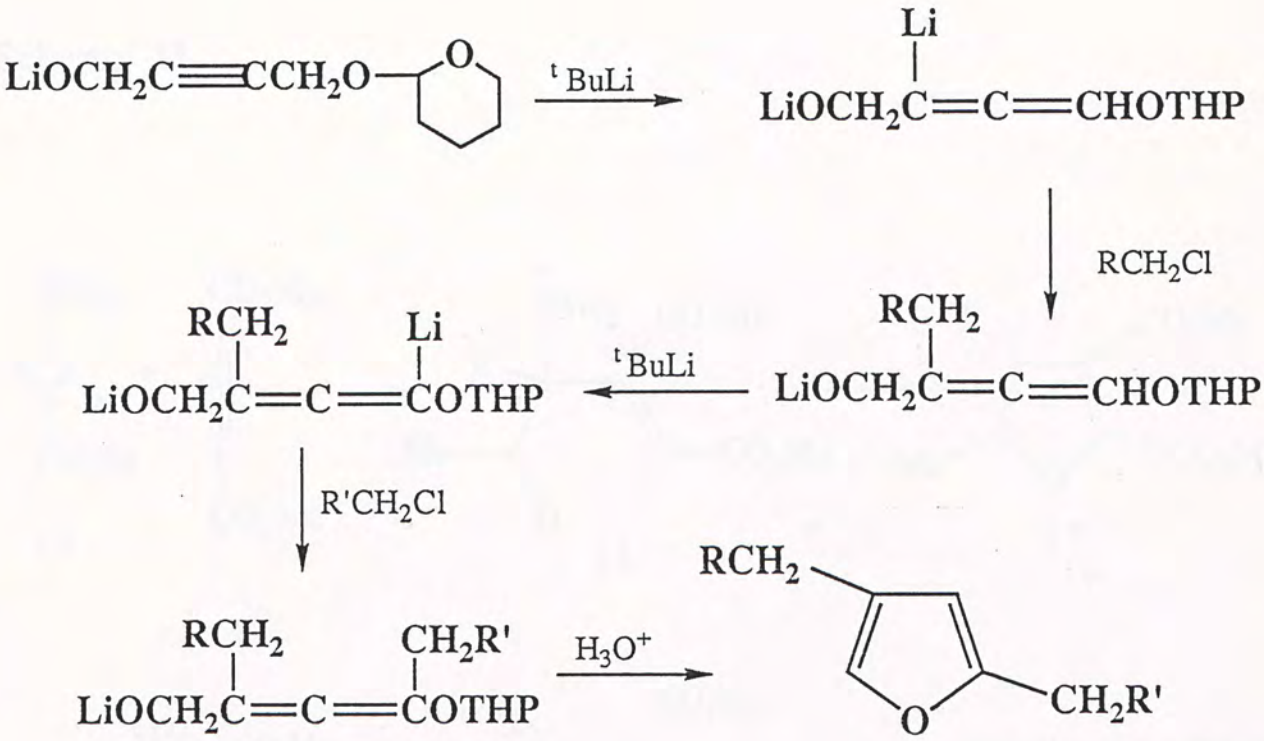
Scheme 9



Dipropynyl ethers offer excellent opportunities for the synthesis of furans because they already contain the oxygen atom along with the right degree of unsaturation. Cyclization is effected with strong bases, and the products show a considerable diversity controlled by the nature of the terminal substituents.

Staehle and Schlosser[31] began with 2-butyne-1,4-diol, by protecting one of the hydroxy group with a tetrahydropyranyl residue and lithiated the other one. After sequential treatments with tert-butyllithium which produce an allenic system in which two alkyl groups are introduced before cyclization to a 2,4-disubstituted furan (Scheme 10).

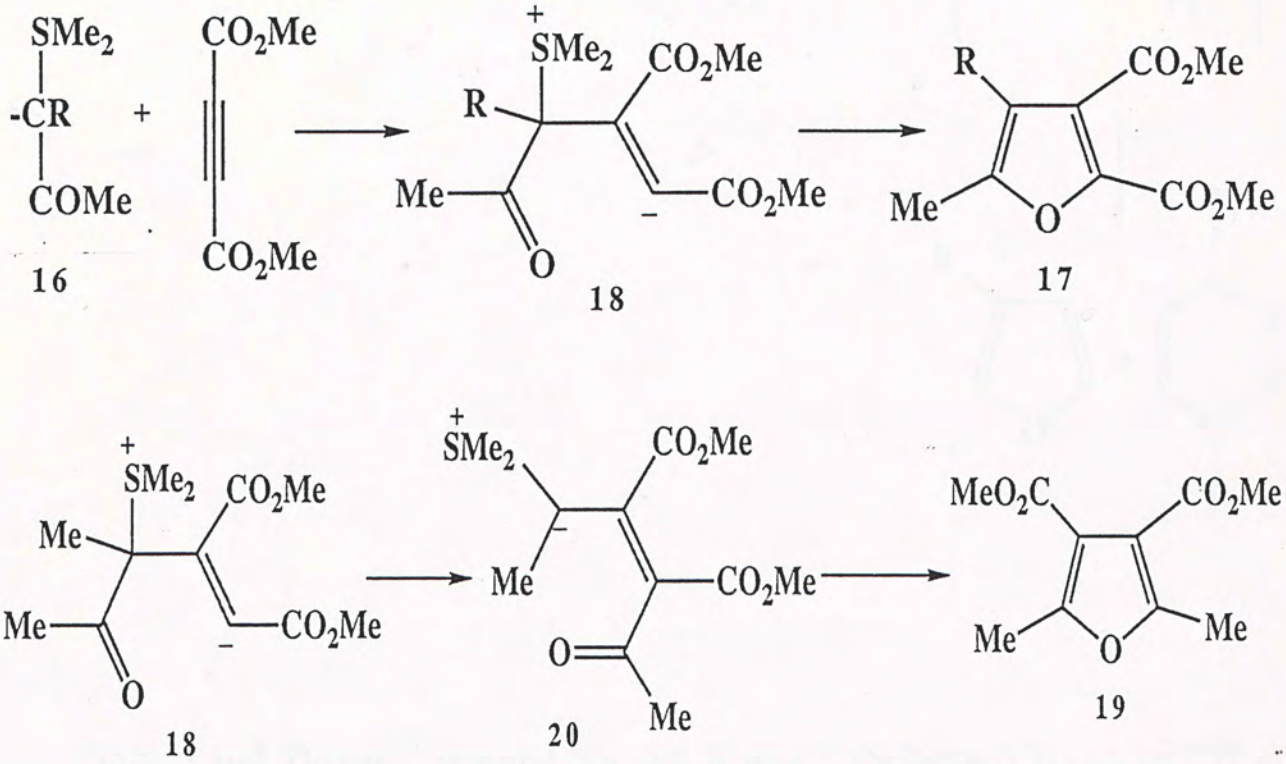
Scheme 10



Dimethyl acetylenedicarboxylate has found to be very useful in furan chemistry. In addition to compounds such as benzoin, a number of compounds undergo base-catalyzed reactions and offer a good route to 2,3-diarylfurans[32]. Japanese chemists have made use of the superior leaving-group abilities of sulfonium sulfur to produce acylated furans (Scheme11); diacylmethylides **16** react with dimethyl acetylenedicarboxylate to give acylated furans **17** at 170°C, perhaps via the cyclization of **18**[33]. The reaction proceeds at ordinary temperatures in dimethyl sulfoxide, but acyl migrations may occur. Thus the ylide is attacked to give the 3,4-dicarboxylate **19**. The intermediate rearranegment product **20** can be isolated before it cyclizes to the furan[34]. The method has been extended to the preparation of 5-methylfuran-2,3,4-tricarboxylic acid and modified by the use of selenium

instead of sulfur ylides[35].

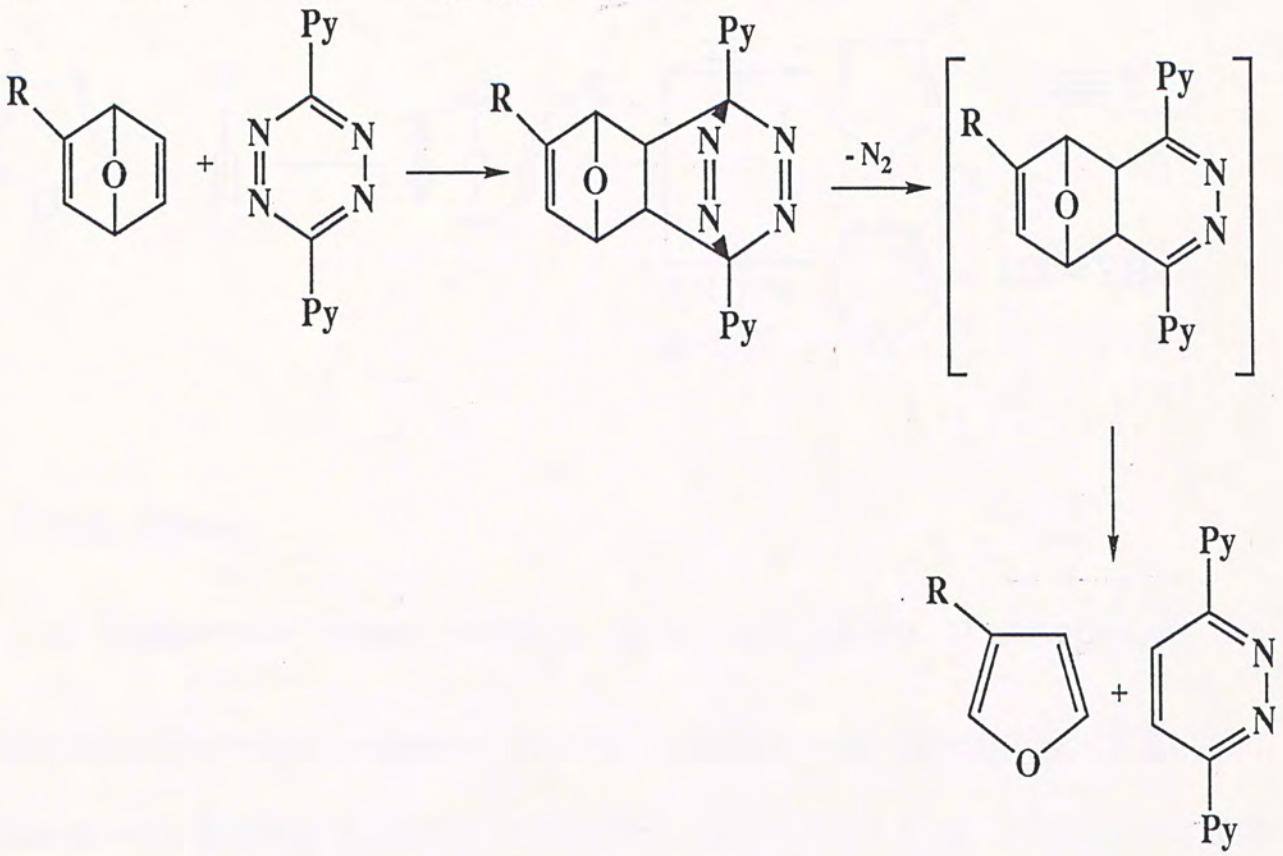
Scheme 11



E. From cycloaddition reactions

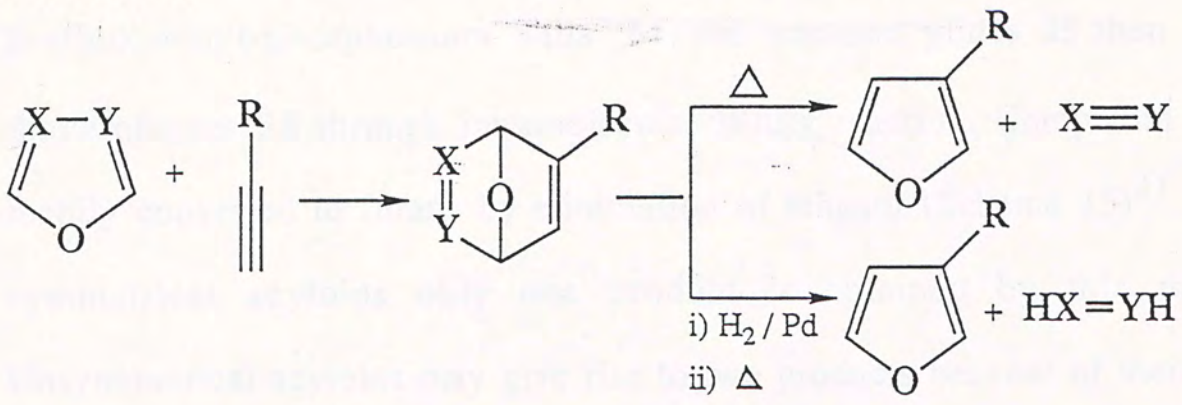
Some kinds of cycloaddition-fragmentation reactions have been described in the synthesis of furans. Wilsons and Warrener[36] have developed a method for conducting the fragmentation stage at ordinary temperature. The cycloaddition product (a 7-oxanorbornadiene) is allowed to add to a disubstituted 1,2,4,5,-tetrazine whereupon nitrogen is eliminated immediately followed by a 1,2-diazine (Scheme 12).

Scheme 12



Ohlson and Turner[37] pointed out that X and Y (Scheme 13) can be CH in which case hydrogenation is needed and the fragmentation has to extrude an alkene. When X=Y=N, elimination should be easy since nitrogen can be ejected at once, but the oxadiazoles do not add alkynes readily. On the other hand, in cases where X=CPh and Y=N, the addition of alkynes to the oxazoles is easy, and the extrusion of benzonitrile is smooth and gives fair yields of 3-acylfurans from the acylated alkynes (Scheme 13). This method is now in widely used and provides an efficient preparation of many useful furans. For example, furan -3,4-bismethanol[38] has been prepared by this method, although arylalkynes do not add well[39].

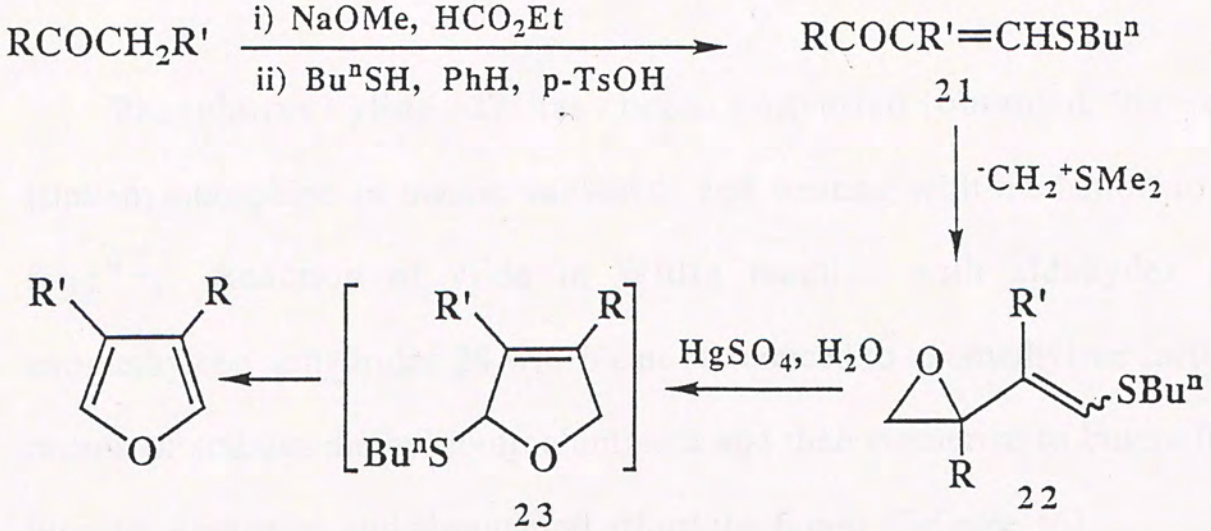
Scheme 13



F. From ylides

α-Hydroxymethylene ketones, from formylation of ketones in the α-position, are readily converted into the corresponding thioenol ethers 21. On reaction with dimethylsulfonium methylide, compound 21 can be converted into oxiranes 22, which can undergo cationic transformation to dihydrofurans 23 and subsequently affords 3,4-disubstituted furans (Scheme 14)[40].

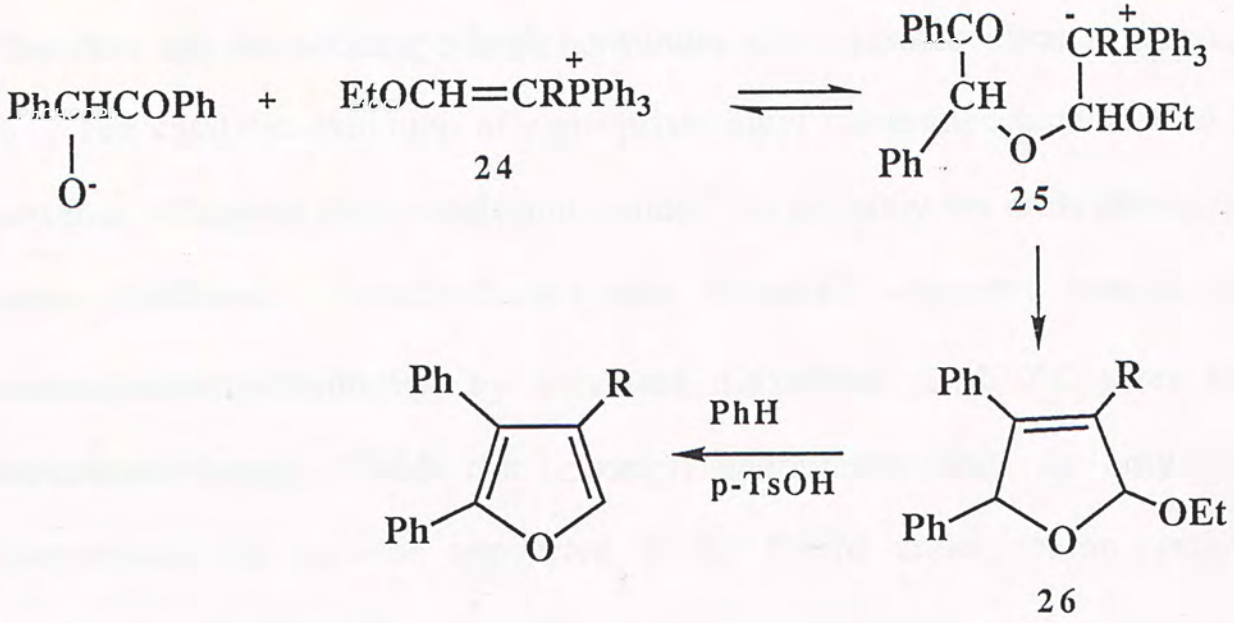
Scheme 14



The anion derived from acyloins undergoes nucleophilic addition to

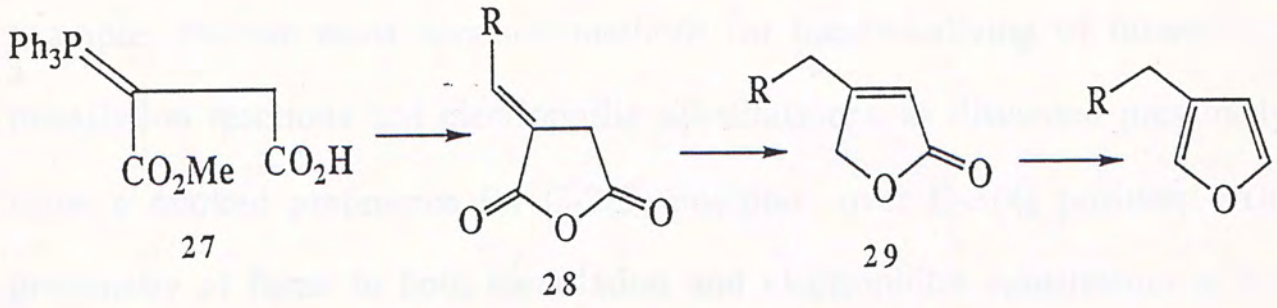
β-ethoxyvinyl-phosphonium salts **24**, the resultant ylides **25** then yields dihydrofurans **26** through intramolecular Wittig reaction. Compound **26** is readily converted to furans by elimination of ethanol (Scheme 15)[41]. With symmetrical acyloins only one product is obtained by this method. Unsymmetrical acyloins may give rise to two products because of their ready tautomerism under basic conditions.

Scheme 15



Phosphorus ylide **27** has been converted (obtained by adding triphenylphosphine to maleic anhydride and treating with methanol) to furan ring[42]. Reaction of ylide in Wittig reaction with aldehydes affords exomethylene anhydrides **28** which can be reduced to exomethylene lactones by means of sodium diethyl-hydroaluminate and then isomerize to butenolides **29** by acid. Reduction and elimination afford the furans (Scheme 16).

Scheme 16



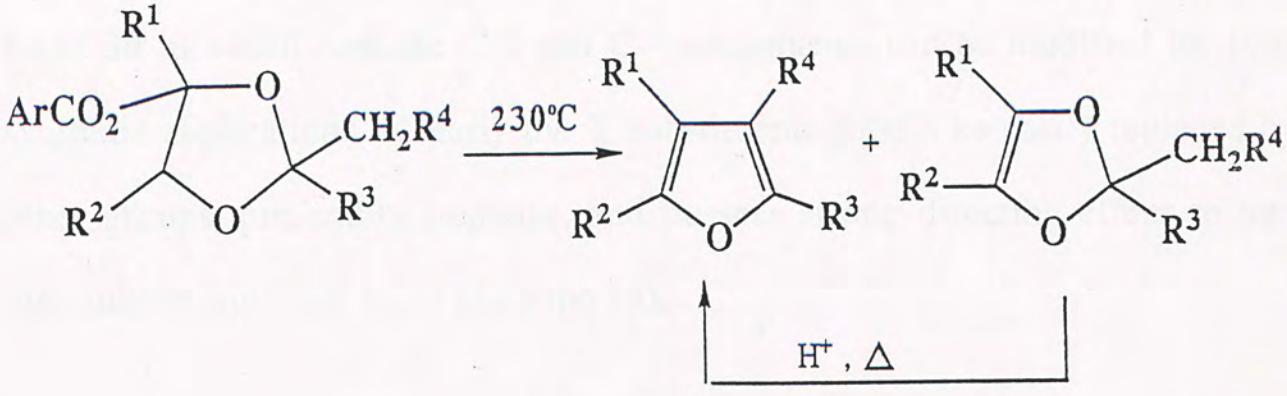
27 28 29

G. From miscellaneous sources

Reduction plus elimination reactions may convert butenolides into furans. Therefore any butenolide synthesis constitutes also a basis for furan synthesis.

The catalytic oxidation of appropriate alkyl substituted butadiene in the presence of copper compounds and iodine[43] is probably the most direct of all furan syntheses. Finally Scharf and Wolters[44] reported that thermal rearrangement-elimination by alkylated dioxolanes at 230°C gives alkyl substituted furans. Yields can be nearly quantitative since the only major by-products can also be converted to the furans under proton-catalyzed thermolysis (Scheme 17).

Scheme 17

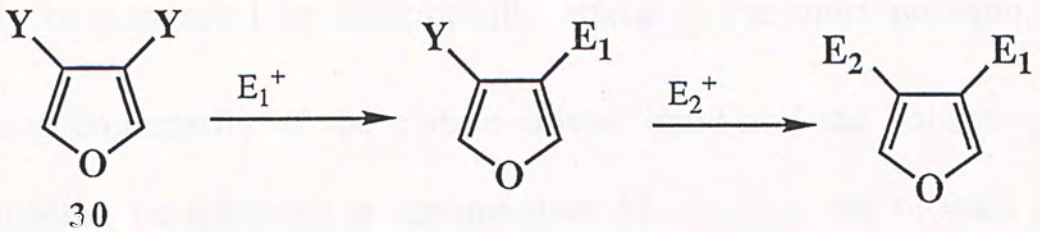


Preparation of 3,4-disubstituted furans is however non-trivial. For example, the two most common methods for functionalizing of furans (i.e., metallation reactions and electrophilic substitutions), as discussed previously, show a marked preference for C-2(5) position over C-3(4) position. The propensity of furan to both metallation and electrophilic substitution at C-2 position or C-5 position has led chemists to develop elaborate methods for preparing 3,4-disubstituted furans. Some of these include chemical modifications of 3,4-bis(acetoxymethyl)furan[45], 3,4-furandicarboxylic acid[46] or 3[(t-butyldimethylsilyl)oxymethyl]furan[47]. Alternative synthetic approaches which do not involve furans as starting materials have also been discussed. These mainly involves the cyclization of acyclic precursors (i.e. Paal-Knorr synthesis, Feist-Benary Synthesis) and Diels-Alder/retro-Diels-Alder chemistry. All these are multi-step processes and the accessibility of starting materials may formulate a problem.

III.3 Aim of the present work

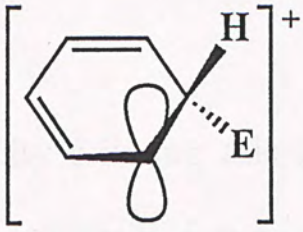
In our continuation of studies in the Diels-Alder reaction between furans and strained alkynes[48], we were interested in synthesizing a 3,4-disubstituted furan **30** in which both the C-3 and C-4 substituents can be modified for later synthetic applications. Clearly the Y substituents should be easily replaced by other groups, preferably stepwise, and possess strong directing effect so that *ipso*-substitution may occur (Scheme 18).

Scheme 18

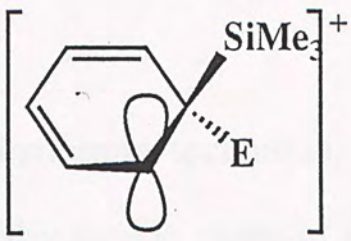


30

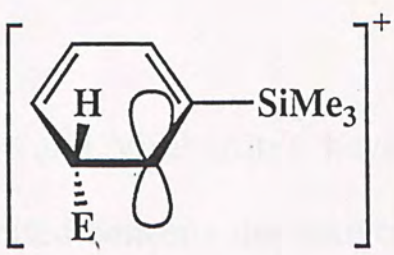
It is well known that arylcarbon-silicon bonds are readily cleaved by a variety of electrophilic reagents[49]. The most attractive feature of arylsilanes is the *ipso*-desilylation when it reacts with electrophilic reagents. This kind of substitution was extensively studied by Eaborn[50] and led to the conclusion that such cleavages occur by the same mechanism as that of electrophilic aromatic substitution. The difference between these reactions are that in the second step where a carbon-silicon bond is broken in the sense of C^-Si^+, rather than a carbon-hydrogen in the direction of C^-H^+. While aromatic substitution involves intermediate delocalized cation **31**, arylsilanes can react via delocalized cations **32**.



31



32

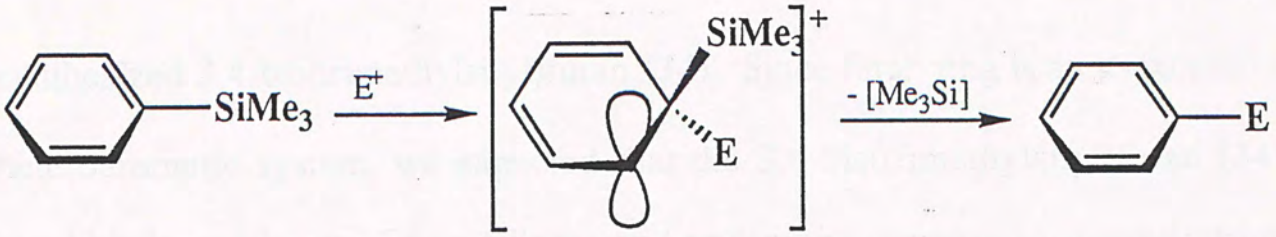


33

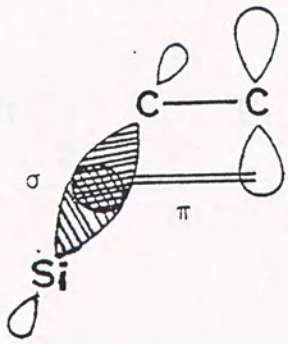
Electrophilic attack occurs at the *ipso* position because of the stabilization offered to an adjacent carbocation by the carbon-silicon bond and this kind of

stabilization is often described as β-effect (Scheme 19). A β-carbocation will certainly be generated by electrophilic attack at the meta position, but the stabilizing coplanarity of the carbon-silicon bond and the vacant p (or π) orbital cannot be achieved in intermediate **33** because the orbitals involved being orthogonal to one another.

Scheme 19



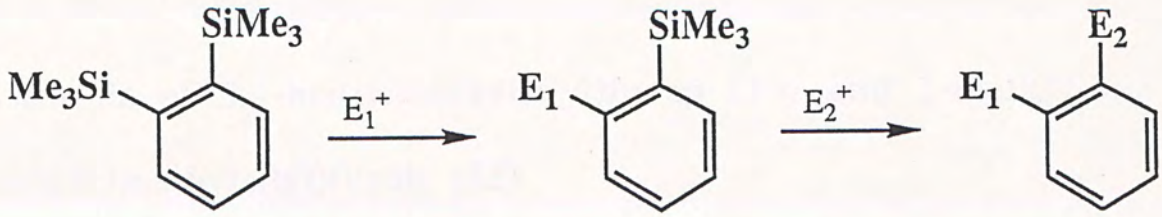
The β-effect:



$(p\text{-}\sigma)_{\pi}$ conjugation

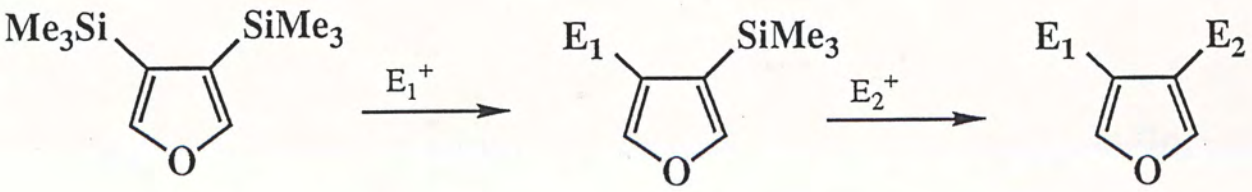
By utilizing this *ipso*-substitution technique, Calas[51] and Vollhardt[52] have synthesized regiospecifically a wide range of disubstituted benzene derivatives by stepwise *ipso*-replacement of the trimethylsilyl groups of bis(trimethylsilyl)-benzenes (Scheme 20).

Scheme 20



Encouraged by these results, we chose the trimethylsilyl group as Y and synthesized 3,4-bis(trimethylsilyl)furan (**34**). Since furan ring is an π-excessive heteroaromatic system, we expected that the 3,4-bis(trimethylsilyl)furan (**34**) would behave like that of arylsilanes and undergoes stepwise *ipso*-substitution when reacting with electrophilic reagents (Scheme 21).

Scheme 21



34

Since furans can readily undergo Diels-Alder reaction, the reaction of 3,4-bis(trimethylsilyl)furan (**34**) with dienophiles has also been studied.

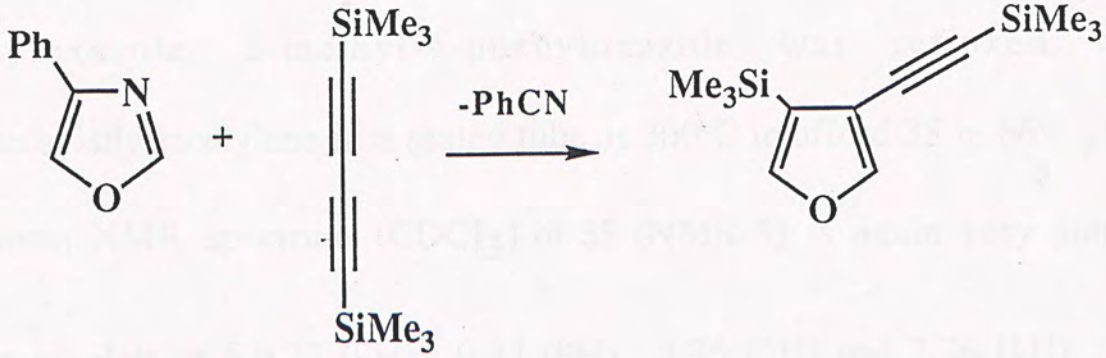
IV. Results and Discussion

A. Synthesis of 3,4-bis(trimethylsilyl)furan (34) and 2-methyl-3, 4-bis(trimethylsilyl)furan (35)

Among all methods for the synthesis of furans, Diels-Alder/retro Diels-Alder reaction would probably be the most direct and efficient method for the preparation of 3,4-disubstituted furans.

It has been known that addition of alkynes to oxazoles gave fair yields of furans[37,41,53]. Our searching for the synthetic pathway was greatly facilitated by the report of Dennis[54] which revealed that the reaction of 4-phenyloxazole with bis-trimethylsilylbuta-1,3-dyne produced the silylated furan (scheme 22).

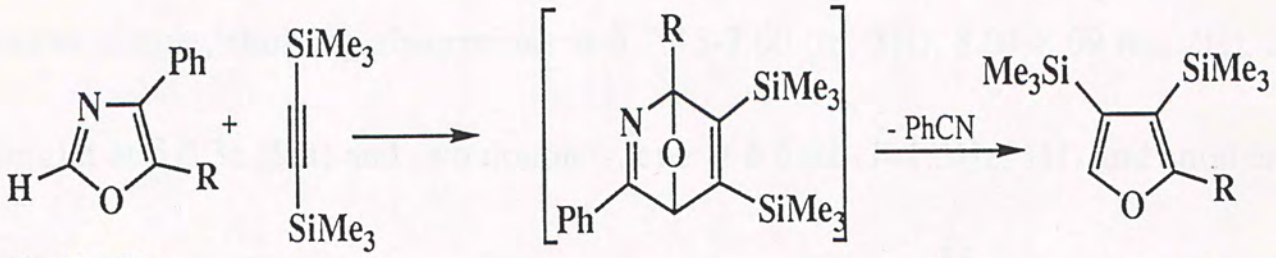
Scheme 22



Scheme 23 shows our strategy for the synthesis of **34** from 4-phenyloxazole[55] and bis(trimethylsilyl)acetylene. The mixture of

4-phenyloxazole and bis(trimethylsilyl)acetylene was heated in a sealed tube at 300°C to afford **34** in 62% yield. The proton NMR spectrum ($CDCl_3$) (NMR-3) of **34** is very simple, showing singlets at δ 0.25 (18H) and 7.37 (2H) which are assigned as the chemical shifts of the methyl protons in trimethylsilyl group and the furan protons, respectively.

Scheme 23



R = H or Me

34 R=H
35 R=Me

Compound **35** was synthesized in the same way as **34**. Instead of 4-phenyloxazole, 5-methyl-4-phenyloxazole was refluxed with bis(trimethylsilyl)acetylene in a sealed tube at 300°C to afford **35** in 66% yield. The proton NMR spectrum ($CDCl_3$) of **35** (NMR-4) is again very simple, showing singlets at δ 0.23 (9H), 0.27 (9H), 2.35 (3H) and 7.26 (1H). The chemical shift of the methyl protons in trimethylsilyl group at C-3 position was assigned to be 0.23 ppm.

B. Acylation-desilylation of 34 and 35

When a mixture of benzoyl chloride and **34** in dichloromethane was treated with aluminium chloride in the same solvent at room temperature, two monodesilylated isomers were obatined. The isomers were easily separated by chromatography, giving a less-polar fraction and a more polar fraction in 62% and 18%, respectively.

The proton NMR spectrum ($CDCl_3$) (NMR-12) of the less polar fraction is rather simple, showing absorptions at δ 7.45-7.60 (m, 3H), 8.04-8.09 (m, 2H), a singlet at δ 0.36 (9H) and two doublets, one at δ 6.62 (J=1.5Hz, 1H) and another at δ 7.63 (J=1.5Hz,1H). According to Batterham (Table 1)[56], J_{34} is 3-4 Hz, J_{35} is 0.7-1 Hz and J_{45} is 1.7-2 Hz, the chemical shifts for C-2(5) proton are around 7.5 ppm, and those the C-3(4) proton are approximately 6-7 ppm.

Table 1 Spectral data for furans[5,6]

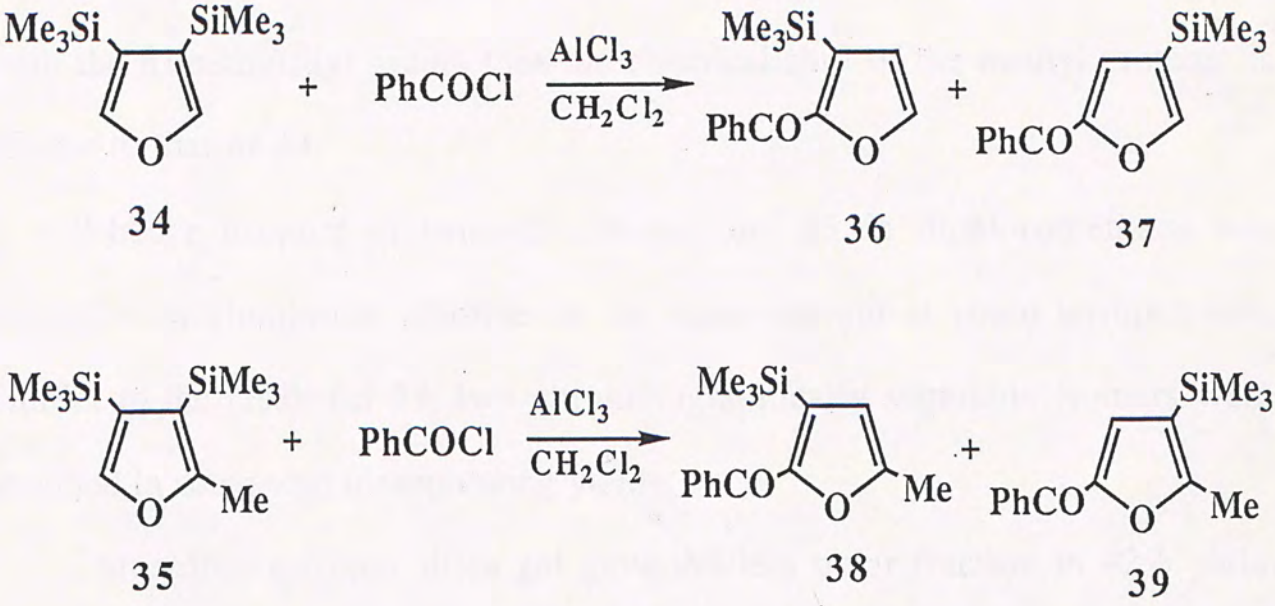
Substitutents	Solvent	δ2	δ3	δ4	δ5	J_{24}	J_{25}	J_{34}	J_{35}	J_{45}
								Hz		
2-Me[a]	CCl_4		5.88	6.18	7.21			3.05	0.95	1.90
2-CHO	CCl_4		7.23	6.61	7.72			3.55	0.80	1.70
2-COMe	CCl_4		7.11	6.53	7.57			3.45	0.75	1.70
2-CO_2Me	CCl_4		7.15	6.52	7.63			3.40	0.85	1.70
2-CH_2NH_2	CCl_4		6.06	6.24	7.28					
3-Me[b]	CCl_4	7.11		6.13	7.23	0.85	1.55			1.75
3-CHO	C_6H_{12}	7.86		6.67	7.31	0.80	1.45			1.90
3-COMe	C_6H_{12}	7.84		6.66	7.26	0.75	1.40			1.80
3-CO_2Me	C_6H_{12}	7.83		6.63	7.24	0.70	1.55			1.85
3-OMe	C_6H_{12}	6.92		6.02	7.01	1.00	1.65			1.90

a. $J_{Me,3}$=0.95Hz, $J_{Me,4}$=0.40Hz, $J_{Me,5}$=0.45Hz

b. $J_{Me,2}$=0.95Hz, $J_{Me,4}$=0.45Hz, $J_{Me,5}$=0.40Hz

By using these informations, we suspected that the less polar fraction is not the expected 3-benzoylated product because of the presence of absorption at δ 6.62. The doublets at δ 6.62 and 7.63 are assigned for the C-4 and C-5 protons respectively, with both chemical shifts and coupling constant in agree with the the assigments of Batterham. Therefore, this product was assigned as 2-benzoyl-3-trimethylsilylfuran (**36**) (Scheme 24).

Scheme 24



For the more polar fraction, the proton NMR spectrum ($CDCl_3$) (NMR-13) shows absorptions at δ 7.46-7.57 (m, 3H), 7.94-7.99 (m, 2H), a singlet at δ 0.26 (9H) and two doublets, one at δ 7.21 (J=0.73Hz,1H) and another at δ 7.59 (J=0.73Hz,1H). Again, we suspected that this compound is not

the expected 3-benzoylated product because of the presence of absorption at δ 7.21. The coupling constants show that the compound is a 2,4-disubstituted furan, the doublet at δ 7.59 is assigned to the C-5 proton. The doublet at δ 7.21 is assigned to the C-3 proton and the deshielding effect of the adjacent benzoyl group might account for the downfield shift of the C-3 proton. This more polar product is therefore assigned as 2-benzoyl-4-trimethylsilylfuran (**37**).

It is noteworthy that the downfield shift of the methyl protons of the trimethylsilyl group in **36** is due to the deshielding effect of the adjacent C-2 benzoyl group. Comparing with **36**, the benzoyl group in **37** is farther apart from the trimethylsilyl group, thus the chemical shift of the methyl protons is similar to that of **34**.

When a mixture of benzoyl chloride and **35** in dichloromethane was treated with aluminium chloride in the same solvent at room termperature. Similar to the result for **34**, two chromatographically separable isomers were obtained in somewhat disappointing yields.

Chromatography on silica gel gave the less polar fraction in 42% yield. The proton NMR spectrum ($CDCl_3$) of which (NMR-14) shows absorption at δ 7.44-7.58(m, 3H), 8.04-8.09(m, 2H), a singlet at δ 0.32 (9H) and two doublets, one at δ 2.40 (J=0.93Hz,3H) and another at δ 6.25 (J=0.93Hz,1H). Obviously, this compound is again not the expected 3-benzoylated product because of the presence of absorption at δ 6.25. The coupling constants suggested that the C-5 methyl protons might couple with the adjacent furan proton, since it has been

reported[56] that the ^4J (allylic) coupling constant between the methyl proton and the C-3 proton is 0.95Hz in 2-methylfuran. This product is therefore assigned as 2-benzoyl-5-methyl-3-trimethylsilylfuran (**38**) (Scheme 24).

The more polar fraction, obtained in 14% yield, shows proton NMR ($CDCl_3$) (NMR-15) absorptions at δ 7.46-7.61 (m, 3H), a doublet at δ 7.92 (J=7.28Hz, 2H) and three singlets at δ 0.26 (9H), 2.48 (3H), and 7.09 (1H). Again, the expected 3-benzoylated product would not exhibit such an absorption pattern. Comparing with that in **38**, the furan proton in this isomer shows a downfield shift and also the ^4J coupling between the C-5 methyl proton and the furan proton was not observed. Therefore, we ascribe the singlet at δ 7.09 to the furan proton which is adjacent to the benzoyl group presumably in accord to the aforementioned argument. Although the ^5J coupling constant between the methyl proton and the C-4 proton is 0.45Hz in 2-methylfuran[56], our NMR spectrometer probably cannot resolve such small coupling constant. This isomer is then assigned as 2-benzoyl-5-methyl-4-trimethylsilylfuran (**39**).

In summary, steric and electronic effects presumably play an important role in preventing the *ipso* attack of the acylium ion and therefore not surprisingly, the acylation reaction occurs at the usual α-position. Kutney[57] also suggested that the site of attack was dependent not only on reactivities but also on relative steric bulk of the 3-alkyl group and/or the entering electrophile.

It was interesting that when the benzoylation-desilylation of **34** was carried out at 0°C, the ratio between **36** and **37** changed from 3.4:1 to 1:1. However

such a ratio change was not observed in the case of **35**. In addition, in the absence of aluminium chloride, the mixture of **34** and benzoyl chloride in dichloromethane at room temperature did not react even after stirring for 4 days (monitored by TLC).

The mono-silylated furans **36,37,38,39** are all quite inert towards further Friedel-Crafts type substitution-desilylation. as such, all mono-silylated furans did not react with benzoyl chloride and acetyl chloride in the presence of aluminium chloride even though the mixture was refluxed in dichloromethane for 24 h.

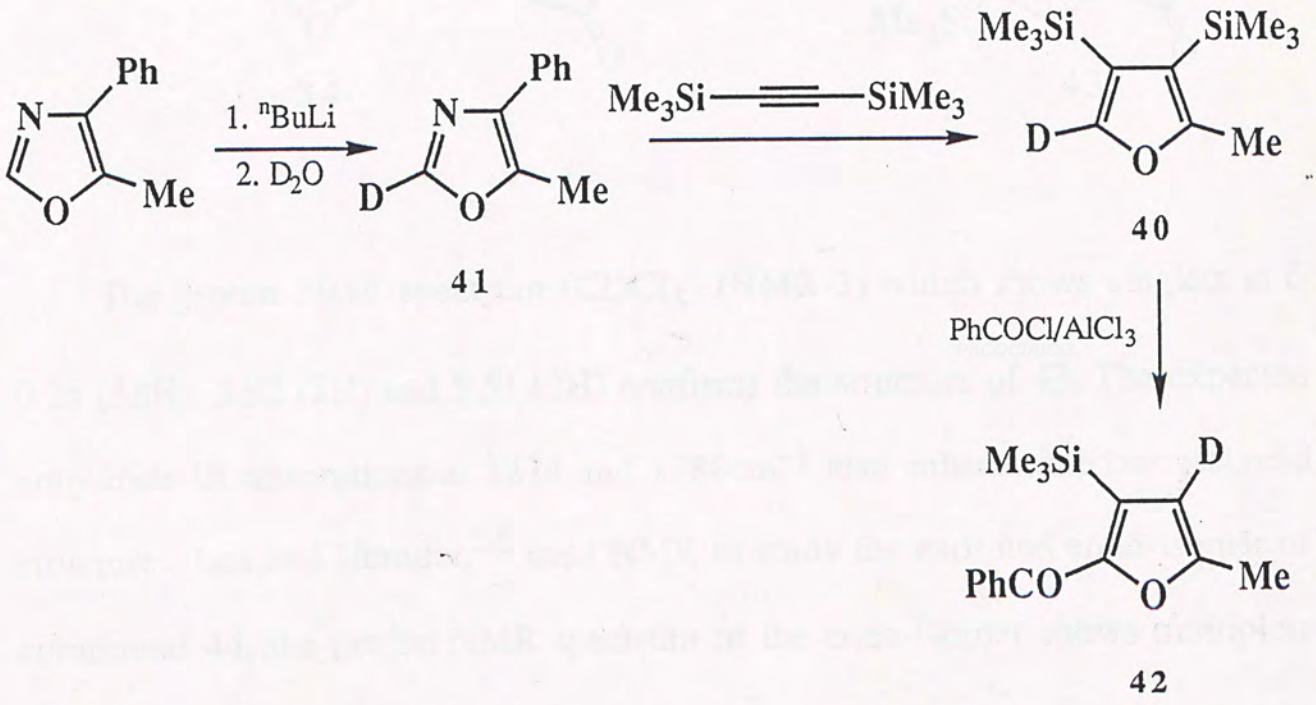
Vollhardt[51] also reported that the first displacement of a silyl group in bis(trimethylsilyl) benzenes occurred more rapidly than the second towards electrophiles. He suggested that steric acceleration might account for such observations.

C. Deuterium Labelling Studies

From the results of the above section, it was observed that one of the trimethylsilyl group should be replaced by a hydrogen atom in order to give the observed products. In order to gain a partial understanding of the mechanism of the aforementioned acylation-desilylation process, we have prepared 2-deuterio-5-methyl-3,4-bis(trimethysilyl)furan (**40**). Unfortunately, direct deprotonation of **35** with n-butyllium, followed by quenching with deuterium oxide failed to afford **40**. Therefore we have to start from 5-methyl-4-phenyloxazole (Scheme 25), 2-deuterio-5-methyl-4-phenyloxazole

(**41**) was prepared by deprotonation of 4-phenyloxazole with n-butyllithium, and was followed by quenching with deuterium oxide. Fortunately, this reaction afforded **41** in 75% yield with 46% D incorporation (as measured from the integration of the NMR spectrum) (NMR-10). Diels-Alder reaction between **41** and bis(trimethylsilyl)acetylene gave **40** in 61% yield. As expected, Friedel-Crafts acylation converted **40** to 2-benzoyl-4-deuterio-5-methyl-3-trimethylsilylfuran (**42**) in 38% yield with 47% D incorporation. From this study, it is likely that the acylation proceeds with intramolecular migration of protons (deuterium) (Scheme 25).

Scheme 25



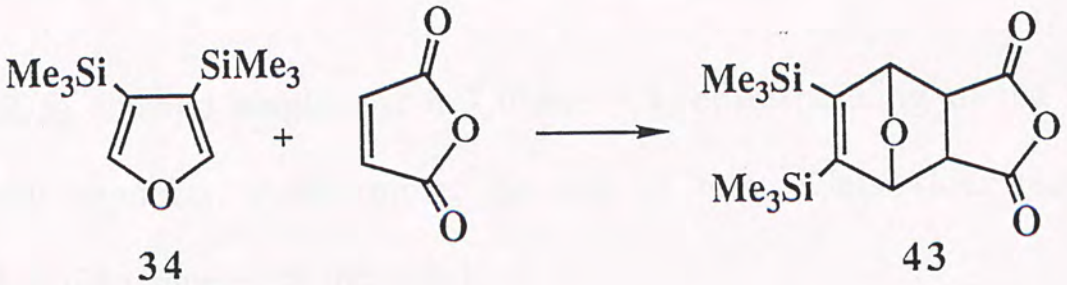
42

D. Diels-Alder reaction of 3,4-bis(trimethylsilyl)furan (34)

It was of particular interest to study the Diels-Alder reaction between furans and strained alkynes. In this context, the Diels-Alder cycloadditions of **34** as diene were investigated.

Diene **34** was allowed to react with methyl fumarate, ethyl maleate and maleic anhydride, only maleic anhydride gave the expected 4,5-bis(trimethylsilyl)-3,6-endoxo-1,2,3,6-tetrahydrophthalic anhydride (**43**) in 40% yield (Scheme 26).

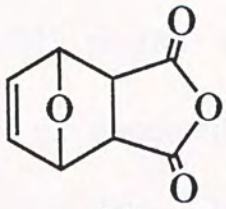
Scheme 26



34 **43**

The proton NMR spectrum ($CDCl_3$) (NMR-5) which shows singlets at δ 0.25 (18H), 2.92 (2H) and 5.51 (2H) confirms the structure of **43.** The expected anhydride IR absorptions at 1874 and 1788cm^{-1} also substantiate our assigned structure. Lee and Herndon[58] used NMR to study the exo- and endo-isomer of compound **44**, the proton NMR spectrum of the endo-isomer shows multiplets at δ 6.5 (2H), 5.4 (2H), 3.9(2H). However, the proton NMR spectrum of the exo-isomer shows multiplets at δ 6.3 (2H), 5.3 (2H) and a singlet at δ 3.2 (2H). Their results showed that there was no coupling between the methine protons

and the oxygen bridge-head protons in the exo-isomer. By using the same argument, compound **43** should be an exo-isomer.



44

Compound **43** was found to be rather unstable in chloroform and gave retro Diels-Alder products. This result was observed when a freshly prepared sample of **43** in $CDCl_3$ was left over-night. Thereupon, the NMR spectrum of **43** (NMR-5) showed singlets at δ 7.0 and 7.4, corresponding to the retro Diels-Alder products. Furthermore, the rate of retro Diels-Alder reaction increased as the temperature increased.

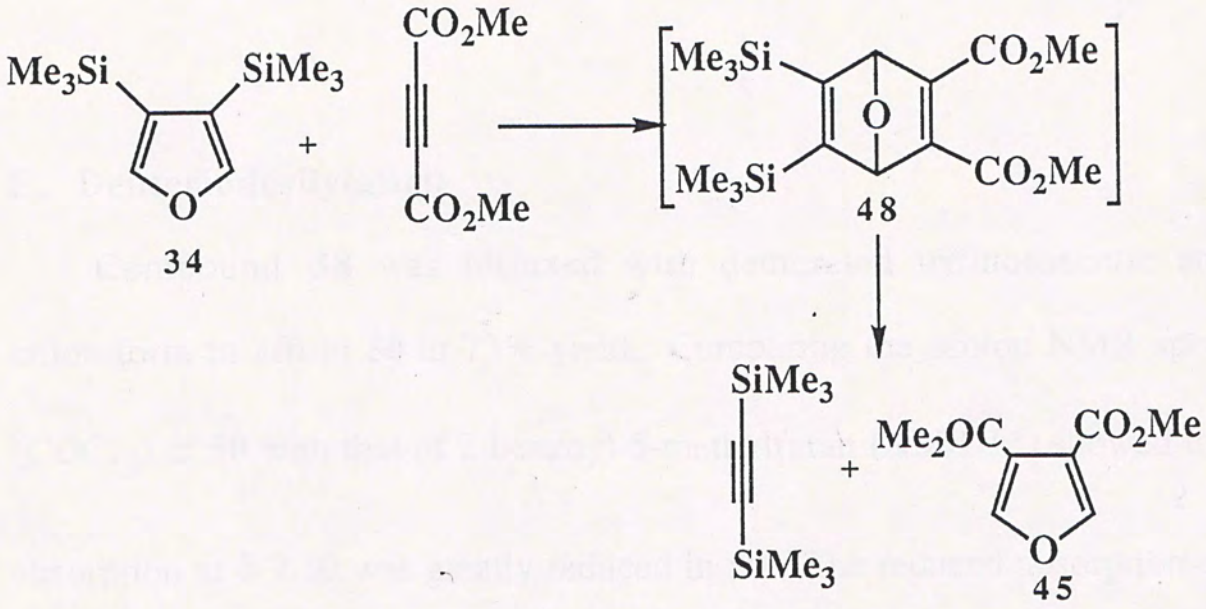
In addition, **43** slowly decomposed at room temperature even in solid form. The decomposition was observed from the fact that aged sample of **43** gave white residue in chloroform while freshly prepared **43** completely dissolved.

When **34** was allowed to react with dimethyl acetylenedicarboxylate, chromatography gave **45** in 73% yield. The proton NMR spectrum ($CDCl_3$) (NMR-6) of the product showed singlets at δ 3.83 (6H) and 7.92 (2H). It was obvious that the product obtained was not the expected adduct and other physical data confirmed the product as dimethyl furan-3,4-dicarboxylate (**45**) (Scheme 27).

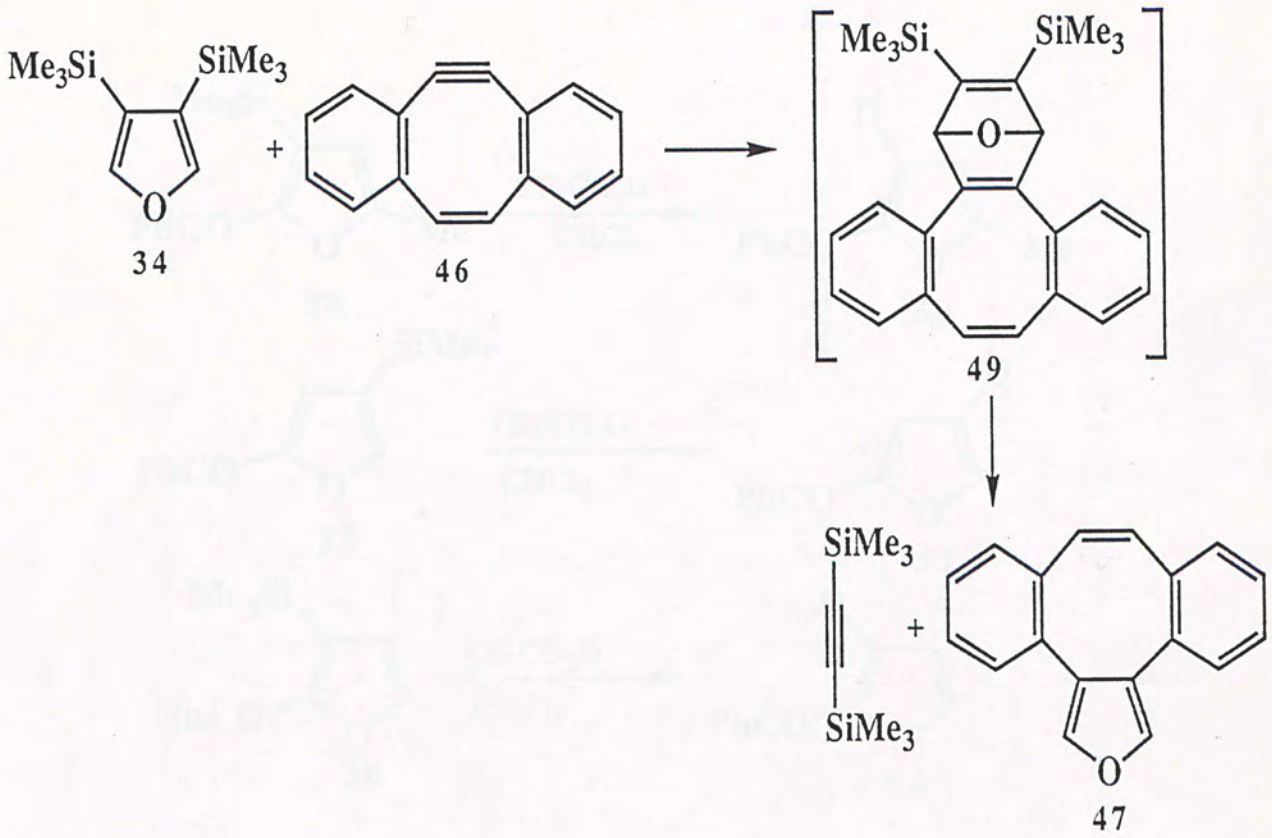
When **34** was treated with 5,6-didehydrodibenzo [*a*,*e*] cyclooctene (**46**), the product obtained gave the proton NMR spectrum($CDCl_3$) (NMR-9) with absorptions at δ 7.16-7.30 (8H), singlets at δ 6.71 (2H) and 7.40 (2H). Again, the product obtained was not the expected adduct and 3,4,7,8-dibenzocycloocta [1,2-*c*]furan (**47**) was assigned as the product (Scheme 27).

The formation of **45** and **47** was presumably through extrusion of bis(trimethylsilyl)acetylene accordingly from the intermediates **48** and **49** (Scheme 27).

Scheme 27



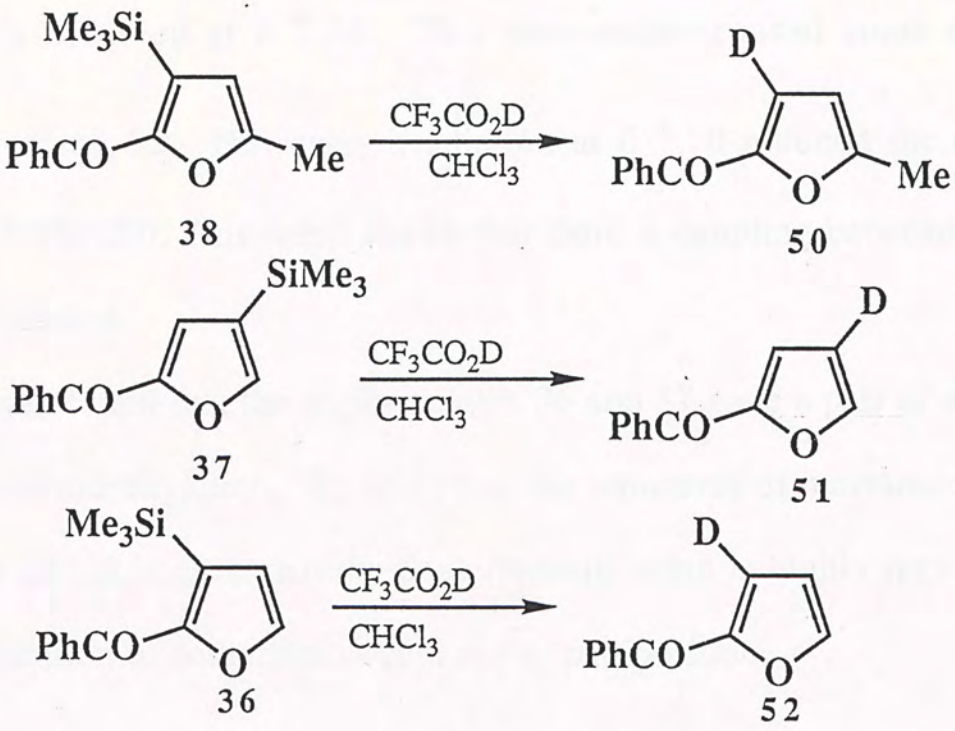
Scheme 27 (cont'd)



E. Deuteriodesilylation

Compound **38** was refluxed with deuterated trifluoroacetic acid in chloroform to afford **50** in 73% yield. Comparing the proton NMR spectrum ($CDCl_3$) of **50** with that of 2-benzoyl-5-methylfuran (NMR-16) showed that the absorption at δ 7.10 was greatly reduced in **50**. The reduced absorption can be assigned to the C-3 proton, therefore we concluded that the deuterium was incorporated to the C-3 position and gave 2-benzoyl-3-deuterio-5-methylfuran (**50**). Since **38** (Scheme 28) contained a trimethylsilyl group at C-3, the result showed that the deuteriodesilylation of **38** was very regiospecific.

Scheme 28



Compound **37** was refluxed with deuterated trifluoroacetic acid in chloroform to afford **51** in 94% yield. Similarly, **52** was synthesized from **36** in quantitative yield. The proton NMR spectra of **51** and **52** are very similar (NMR-19) except that the absorption at δ 7.24 is greatly diminished in **52** while the reduced absorption occurs at δ 6.60 in **51**. It is reasonable that the absorption at δ 7.24 is assigned to C-3 proton, which is adjacent to the benzoyl group, and the absorption of C-4 proton occurs at δ 6.60. Therefore we concluded that the deuterium attacked the C-3 position of compound **36** and C-4 position of compound **37**, resulting in the formation of 2-benzoyl-3-deuteriofuran (**52**) and 2-benzoyl-4-deuteriofuran (**51**),

respectively.

In the proton NMR spectrum of **52**, a doublet is observed at δ 6.60 while a singlet is observed at δ 7.70. This observation caused some doubt in the assignment of **52**. However, irradiation at δ 7.70 reduced the doublet to a singlet (NMR-20). This reuslt shows that there is coupling between the C-4 and the C-5 protons.

It was found that the regio-isomers **36** and **37** gave a pair of regio-isomers after deuteriodesilylation. By analyzing the structures of reactants and products (Scheme 28), it is clear that the deuteriodesilylation is highly regiospecific and the substitution of deuterium occurs at the *ipso* position.

V. Conclusion

The synthesis of 3,4-bis(trimethylsilyl)furan (34) and 2-methyl-3,4-bis(trimethylsilyl)furan (35) via oxazoles has been achieved. Since the oxazoles provides C-2 and C-5 substituents in the furan ring, a large number of 3,4-bis(trimethylsilyl)furans might be synthesized via similar strategy.

3,4-bis(trimethylsilyl)furan (34) is able to undergo Diels-Alder reaction with dienophiles although the reactivity is lower than the similar diene reported by Garratt[59]. For acetylenic dienophiles, extrusion of bis(trimethylsilyl)-acetylene occurs and this may formulate a viable route for the synthesis of annulated furans.

The synthesized 3,4-bis(trimethylsilyl)furans 34 and 35 are able to undergo regiospecific electrophilic substitution at the unsubstituted α-position. Furthermore, the Friedel-Crafts products can be converted to deuterated compounds, with deuterium atom substituting the trimethylsilyl group. It is thus anticipated that the same strategy can be applied to the realization of polysubstituted furans.

VI. Experimental Section

Solvents used were purified by standard procedures. All evaporation of organic solvents was carried out by a rotary evaporator in conjunction with a water aspirator.

Proton NMR spectra were recorded on a Bruker Cryospec WM 250 (250MHz) spectrometer or a Jeol PMX 60SI (60MHz) spectrometer. The chemical shift (ppm) was measured with tetramethylsilane (TMS) serving as internal standard and deuterated chloroform was used as solvent unless stated otherwise. Mass spectra were recorded on a VG Micromass 7070F spectrometer. IR spectra were run on a Perkin-Elmer Infrared Spectrophotometer 283. Elemental analyses were carried out at Shanghai Institute of Organic Chemistry, Academia Sinica, China.

Merck silica gel ($60F_{254}$) precoated on aluminium sheet was used for TLC studies and Merck silica gel (70-230 mesh) was used for column chromatography. Preparative TLC was carried out on 1.0 mm thick layers of Merck Kieselgel 60 PF_{254} on 20x20 cm^2 glass plates. Melting points were measured on a hot-stage microscope and were uncorrected.

4-Phenyloxazole

A mixture of ammonium formate (44g, 0.7mol), phenacyl bromide (40g, 0.2mol), anhydrous formic acid (220mL) was refluxed for 3.5 h. The reaction mixture was cooled in an ice bath and NaOH solution (29.3M, 200mL) was added. After cooling, diethyl ether (100mL) was added, the layers were separated and the aqueous layer was extracted with diethyl ether (2x200mL). The ether solution was dried over anhydrous magnesium sulphate. Evaporation of solvent gave a deep brown oil. Vacuum distillation gave 4-phenyloxazole as yellow liquid (7.8g, 27%): b.p 57-60 °C (0.6mmHg) [lit.[55] b.p 111-113°C (10mmHg)].

Mass spectrum: *m/e* 145 (M^+)

^{1}H-NMR (NMR-1): δ7.20-7.40(m, 3H), 7.71-7.75(m, 2H), 7.88(s, 1H), 7.89(s, 1H).

2-Bromopropiophenone

Bromine (40g, 0.25mol) was added dropwise to a stirred solution of propiophenone (33.5g, 0.25mol) in glacial acetic acid (100mL) at 0°C for 3 h. The solvent was evaporated under reduced pressure and vacuum distillation gave 2-bromopropiophenone as pale yellow liquid (47.9, 90%): b.p 80-82°C (0.5mmHg) [lit.[60] b.p 134-135°C (18mmHg)].

5-Methyl-4-phenyloxazole

A mixture of ammonium formate (40g, 0.63mol), 2-bromo-propiophenone (40g, 0.19mol), anhydrous formic acid (220mL) was refluxed for 5 h. The reaction mixture was cooled in an ice bath and NaOH solution (29.3M, 200mL) was added to neutralize the acid. After cooling, diethyl ether (100mL) was then added, the layers were separated and the aqueous layer was extracted with diethyl ether (2x200mL). The ether solution was dried over anhydrous magnesium sulphate. Evaporation of solvent gave a deep brown oil. Vacuum distillation gave 5-methyl-4-phenyloxazole as pale yellow liquid (12.9g, 43%): b.p 58-60 °C (0.3mmHg) [lit.[55] b.p 115-116°C (15mmHg)].

Mass spectrum: *m/e* 159 (M^+)

^{1}H-NMR (60MHz) (NMR-2): δ2.55(s, 3H), 7.23-7.73(m, 5H), 7.78(s, 1H).

3,4-Bis(trimethylsilyl)furan (34)

A mixture of 4-phenyloxazole (4g, 0.03mol) and bis(trimethylsilyl)acetylene (4.8g, 0.03mol) was heat a sealed t t 300°C for 4 day. Vacuum distillation gave a colo ss quid w h ntained benzonitrile and 3,4-bis(trimethylsilyl)furan 0-3 , 0.6 Hg he liquid

was further purified by column chromatography (alumina, grade III, hexanes) to give 3,4-bis(trimethylsilyl)furan (34) as colorless liquid (3.7g, 62%).

Mass spectrum: *m/e* 212 (M^+)

Anal.: Calcd for $C_{10}H_{20}OSi_2$: C 56.54, H 9.49; Found: C 56.19, H 9.55.

^{1}H-NMR (60MHz) (NMR-3): δ0.25(s, 18H), 7.37(s, 2H).

IR spectrum: 2966, 2909, 1813, 1784, 1497, 1271, 1255, 1067, 1042, 1026, 836, 757cm^{-1}.

2-Methyl-3,4-bis(trimethylsilyl)furan (35)

A mixture of 5-methyl-4-phenyloxazole (4g, 0.03mol) and bis(trimethylsilyl)acetylene (4.3g, 0.03mol) was heated in a sealed tube at 300°C for 7 days. Vacuum distillation gave a colourless liquid (40-45°C, 0.6mmHg). The liquid was further purified by column chromatography (alumina, grade III, hexanes) to give 2-methyl-3,4-bis(trimethylsilyl)furan (35) as colorless liquid (3.75g, 66%).

Mass spectrum: *m/e* 226 (M^+)

Anal.: Calcd for $C_{11}H_{22}OSi_2$: C 58.34, H 9.79; Found: C 58.16, H 9.80.

^{1}H-NMR (60MHz) (NMR-4): δ0.23(s, 9H), 0.27(s, 9H), 2.35(s,3H), 7.26(s, 1H).

IR spectrum (KBr): 2966, 2910, 1789, 1547, 1503, 1298, 1254, 1129, 835, 758cm^{-1}.

Exo-4,5-bis(trimethylsilyl)-3,6-endoxo-1,2,3,6-tetrahydrophthalic anhydride (43)

A mixture of 3,4-bis(trimethylsilyl)furan (34) (0.9g, 4.2mmol) and maleic anhydride (0.4g, 4.1mmol) was stirred under N_2 for 4 days. The

resulted yellow precipitate was washed with hexanes until no more solid dissolved. The hexane solution was evaporated and the residual white solid was recrystallized from hexanes at 0°C to afford exo-4,5-bis(trimethylsilyl)-3,6-endoxo-1,2,3,6-tetrahydrophthalic anhydride (**43**) as wool like crystals (522mg, 40%), m.p 83-84°C

Mass spectrum: *m/e* 212 (M^+-98)

Anal.: Calcd for $C_{14}H_{22}O_4Si_2$: C 54.15, H 7.14; Found: C 53.45, H 7.05.

^{1}H-NMR (NMR-5): δ0.25(s, 18H), 2.92(s, 2H), 5.51(s, 2H).

IR spectrum (KBr): 2960, 1874, 1788, 1734, 1593, 1433, 1253, 1231, 1074, 1033, 998, 929, 874, 843, 759, 721cm^{-1}.

Dimethyl furan-3,4-dicarboxylate (45)

A mixture of 3,4-bis(trimethylsilyl)furan (**34**) (110mg, 0.5mmol) and dimethyl acetylenedicarboxylate (120mg, 0.8mmol) was heated in a sealed tube at 75°C for 7 h. The resulted residue was purified by column chromatography (silica gel, EtOAc-hexanes 1:4) to give dimethyl furan-3,4-dicarboxylate (**45**) as white crystals (70mg, 73%), m.p 43-44°C [lit.[61] m.p 46°C].

Mass spectrum: *m/e* 184 (M^+)

^{1}H-NMR (60MHz) (NMR-6): δ3.83(s, 6H), 7.92(s, 2H).

5,6-Dibromo-5,6-dihydrodibenzo[*a,e*]cyclooctene

A solution of bromine (0.78g, 4.88mmol) in dichloromethane (1mL) was added dropwise during a period of 5 min to a solution of dibenzo[*a,e*]cyclooctene (0.78g, 3.82mmol) in dichloromethane (5mL) at 0°C, and the solution was then stirred at 0°C for 20 min. Evaporation of solvent and crystallization from carbon tetrachloride yielded

5,6-dibromo-5,6-dihydrodibenzo[*a*,*e*]cyclooctene as colorless crystals (0.91g, 65%) m.p 155-157°C [lit.[62] 157-159°C].

^{1}H-NMR (60MHz) (NMR-7): δ5.78(s, 2H), 6.90-7.70(m, 10H).

5-Bromodibenzo[*a*,*e*]cyclooctene

A solution of 5,6-bromodibenzo[*a*,*e*]cyclooctene (200mg, 0.6mmol) and 1,5-diazabicyclo[4,3,0]non-5-ene (0.70g, 0.56mmol) in benzene (4mL) was refluxed under N_2 for 2 h. The solution was cooled, washed with 2N H_2SO_4 aq (5mL) and H_2O (5mL). The benzene layer was dried over anhydrous magnesium sulphate. The solvent was evaporated and slow crystallization from ethanol gave 5-bromodibenzo[*a*,*e*]cyclooctene as colorless crystals (110mg, 71%) m.p 74-76°C [lit.[62] 76-78°C].

Mass spectrum (60MHz) (NMR-8): δ6.80(s, 2H), 7.10-7.50(m, 9H).

3,4,7,8-Dibenzocycloocta[1,2-*c*]furan (47)

A solution of 5-bromodibenzo[*a*,*e*]cyclooctene (200mg, 0.7mmol) in dry tetrahydrofuran (2mL) was added dropwise during a period of 2 min to a stirred solution of KO^{t}Bu (240mg, 2.2mmol) in dry tetrahydrofuran (20mL) at room temperature under N_2. The solution was stirred for 5 min, 2N aq HCL (10mL) was added and the solution was extracted with diethyl ether (2x10mL). The organic layer was washed with H_2O (5mL) and dried over anhydrous magnesium sulphate. Evaporation and chromatography (alumina, grade III, hexanes) gave out a yellow solution which contained 5,6-didehydrodibenzo[*a*,*e*]cyclooctene (**46**). 3,4-Bis(trimethylsilyl)furan (**34**) (200mg, 0.94mmol) was then added to the yellow solution. The mixture was concentrated to 5mL and stirred under N_2 for 2.5 days. Preparative TLC (hexanes) gave 3,4,7,8-dibenzocycloocta[1,2-*c*]furan (**47**) as white solid (6mg,

3%) m.p 113-116°C.

Mass spectrum: *m/e* 244 (M^+)

Exact mass: Calcd for $C_{18}H_{12}O$, 244.0888; Found: 244.0861.

^{1}H-NMR (NMR-9): δ6.71(s, 2H), 7.16-7.30(m, 8H), 7.40(s, 2H).

2-Deuterio-5-methyl-4-phenyloxazole (41)

To a solution of 5-methyl-4-phenyloxazole (2.2g, 9.7mmol) in dry diethyl ether (30mL), n-butyl lithium (0.86g, 14.4mmol) was added during a period of 5 min. The mixture was stirred at room temperature under N_2 for 15min, and D_2O (10mL) was added slowly. The organic layer was dried over anhydrous magnesium sulphate, evaporation and chromatography (silica gel, EtOAc-hexanes 3:38) gave 2-deuterio-5-methyl-4-phenyloxazole (**41**) as yellow liquid (1.67g, 75%).

Mass spectrum: *m/e* 160 (M^+, 100%), (M^+-1, 94%)

^{1}H-NMR (NMR-10): δ2.55(s, 3H), 7.28-7.56(m, 3H), 7.64-7.69(m, 2H).

2-Deuterio-5-methyl-3,4-bis(trimethylsilyl)furan (40)

A mixture of 2-deuterio-5-methyl-4-phenyloxazole (**41**) (1.6g, 0.01mol) and bis(trimethylsilyl)acetylene (1.7g, 0.011mol) was heated in a sealed tube at 300°C for 7 days. Vacuum distillation gave a colorless liquid (50°C, 0.8mmHg). The liquid was purified by column chromatography (alumina, grade III, hexanes) to provide 2-deuterio-5-methyl-3,4-bis(trimethylsilyl)furan (**40**) as colorless liquid (1.1g, 61%).

Mass spectrum: *m/e* 227(M^+, 4.8%), (M^+-1, 4.4%)

Exact mass: Calcd for $C_{11}H_{21}DOSi_2$, 227.1272; Found: 227.1233.

^{1}H-NMR (60MHz, CCl_4) (NMR-11): δ0.23(s, 9H), 0.27(s, 9H), 2.32(s,3H).

2-Benzoyl-4-deuterio-5-methyl-3-trimethylsilylfuran (42)

To a solution of aluminium chloride (320mg, 2.4mmol) in dichloromethane (3mL), a mixture of 2-deuterio-5-methyl-3,4-bis(trimethylsilyl)furan (**40**) (452mg, 2mmol) and benzoyl chloride (280mg, 2.0mmol) in dichloromethane (4mL) was added, the solution was stirred at room temperature under N_2 for 3 h. Icy water (20mL) was then added, the layers were separated and the aqueous layer was extracted with dichloromethane (2x30mL). The dichloromethane solution was dried over anhydrous magnesium sulphate. Evaporation and chromatography (alumina, grade III, hexanes) gave a yellow liquid. Crystallization in hexanes at -20°C gave 2-benzoyl-4-deuterio-5-methyl-3-trimethylsilylfuran (**42**) as coloress crystals (196mg, 38%). m.p 58-59°C.

Mass spectrum: *m/e* 259 (M^+, 2.1%), (M^+-1, 3.7%)

Exact mass: Calcd for $C_{15}H_{17}DO_2Si$, 259.1139; Found: 259.1114.

^{1}H-NMR (NMR-11): δ2.40(s,3H), 7.44-7.59(m,3H), 8.04-8.09(m, 2H).

2-Benzoyl-3-trimethylsilylfuran (36) and
2-Benzoyl-4-trimethylsilylfuran (37)

To a solution of aluminium chloride (250mg, 2mmol) in dichloromethane (3mL), a mixture of 3,4-bis(trimethylsilyl)furan (**34**) (300mg, 1.5mmol) and benzoyl chloride (210mg, 1.5mmol) in dichloromethane (4mL) was added, the solution was stirred at room temperature under N_2 for 3 h. Icy water (10mL) was then added , the layers were separated and the aqueous layer was extracted with dichloromethane (2x20mL). The dichloromethane solution was dried over anhydrous magnesium sulphate. Evaporation and

chromatography (alumina, grade III, hexanes) gave two major portions. The less polar portion was 2-benzoyl-3-trimethylsilylfuran (**36**) as pale yellow liquid (150mg, 62%).

Mass spectrum: *m/e* 229 (M^+-15)

Anal.: Calcd for $C_{14}H_{16}O_2Si$: C 68.81, H 6.60; Found: C 68.72, H 6.84

^{1}H-NMR (NMR-12): δ0.36(s, 9H), 6.62(d, J=1.5Hz, 1H), 7.45-7.60(m,3H), 7.63(d, J=1.5Hz, 1H), 8.04-8.09(m, 2H).

IR spectrum (KBr): 3072, 2961, 1693, 1450, 1413, 1371, 1340, 1266, 1178, 1070, 886, 841, 760, 712cm^{-1}

Further chromatography of the more polar portion (silica gel, EtOAc-hexanes 1:6) and recrystallization from hexanes at -20°C gave 2-benzoyl-4-trimethylsilylfuran (**37**) as colorless crystals (44mg, 18%), m.p 44-45°C.

Mass spectrum: *m/e* 244 (M^+)

Anal.: Calcd for $C_{14}H_{16}O_2Si$: C 68.81, H 6.60; Found: C 68.51, H 6.40.

^{1}H-NMR (NMR-13): δ0.26(s, 9H), 7.21(d, J=0.73Hz, 1H), 7.46-7.57(m, 3H), 7.59(d, J=0.73Hz, 1H), 7.94-7.99(m, 2H).

IR spectrum (KBr): 3124, 3077, 2958, 1631, 1550, 1472, 1336, 1326, 1314, 1290, 1252, 1218, 1193, 1096, 876, 841, 791, 755, 714cm^{-1}.

2-Benzoyl-5-methyl-3-trimethylsilylfuran (38) and 2-Benzoyl-5-methyl-4-trimethylsilylfuran (39)

To a solution of aluminium chloride (320mg, 2.4mmol) in dichloromethane (3mL), a mixture of 2-methyl-3,4-bis(trimethylsilyl)furan (**35**) (452mg, 2mmol) and benzoyl chloride (280mg, 2mmol) in dichloromethane (4mL) was added, the solution was stirred at room

temperature under N_2 for 3h. Icy water (20mL) was then added , the layers were separated and the aqueous layer was extracted with dichloromethane (2x30mL). The dichloromethane solution was dried over anhydrous magnesium sulphate. Evaporation and chromatography (alumina, grade III, hexanes) gave two major portions. Recrystallization of the less polar portion from hexanes at -20°C gave 2-benzoyl-5-methyl-3-trimethylsilylfuran (**38**) as colorless crystals (217mg, 42%), m.p 58-59°C.

Mass spectrum: *m/e* 258 (M^+)

Exact mass: Calcd for $C_{15}H_{18}O_2Si$, 258.1076; Found: 258.1061

Anal.: Calcd for $C_{15}H_{18}O_2Si$: C 69.72, H 7.02; Found: C 69.67, H 6.86

^{1}H-NMR (NMR-14): δ0.32(s, 9H), 2.40(d, J=0.93Hz, 3H), 6.25(d, J=0.93Hz, 1H), 7.44-7.58(m, 3H), 8.04-8.09(m, 2H).

Further chromatography of the more polar portion (silica gel, EtOAc-hexanes 2:13) and recrystallization from hexanes at -20°C gave 2-benzoyl-5-methyl-4-trimethylsilylfuran (**39**) as colorless crystals (67mg, 14%), m.p 63-64°C.

Mass spectrum: *m/e* 258(M^+)

Exact mass: Calcd for $C_{15}H_{18}O_2Si$, 258.1076; Found: 258.1057.

Anal.: Calcd for $C_{15}H_{18}O_2Si$: C 69.72, H 7.02; Found: C 69.88, H 7.10.

^{1}H-NMR (NMR-15): δ0.26(s, 9H), 2.48(s, 3H), 7.09(s, 1H), 7.46-7.61(m, 3H), 7.92(d, J=7.28Hz, 2H).

IR spectrum (KBr): 3070, 2959, 2905, 1640, 1599, 1503, 1451, 1345, 1286, 1251, 1192, 1175, 1010, 890, 757, 725cm^{-1}.

2-Benzoyl-5-methylfuran

A mixture of 2-benzoyl-5-methyl-3-trimethylsilylfuran (**38**) (130mg, 0.5mmol) in chloroform (2mL) and trifluoroacetic acid (1mL) was refluxed for 4 days. Evaporation and chromatography (silica gel, EtOAc-hexanes 1:6) gave 2-benzoyl-5-methylfuran as pale yellow liquid (35mg, 81%) and unreacted 2-benzoyl-5-methyl-3-trimethylsilylfuran (**38**) (70mg).

Mass spectrum: *m/e* 186 (M^+)

Exact mass: Calcd for $C_{12}H_{10}O_2$, 186.0681; Found: 186.0679.

^{1}H-NMR (NMR-16): δ2.44(s, 3H), 6.21(d, J=3.5Hz, 1H),
7.10(d, J=3.5Hz, 1H),
7.44-7.60(m, 3H), 7.89-7.93(m,2H).

2-Benzoyl-3-deuterio-5-methylfuran (50)

A mixture of 2-benzoyl-5-methyl-3-trimethylsilylfuran (**38**) (100mg, 0.4mmol) in chloroform (2mL) and deuteriated trifluoroacetic acid (1mL) was refluxed under N_2 for 7 days. Evaporation and chromatography (silica gel, EtOAc-hexanes 1:6) gave 2-benzoyl-3-deuterio-5-methylfuran (**50**) as yellow liquid (39mg, 79%) and unreacted 2-benzoyl-5-methyl-3-trimethylsilylfuran (**38**) (32mg).

Mass spectrum: *m/e* 187 (M^+)

Exact mass: Calcd for $C_{12}H_9DO_2$, 187.0744; Found: 187.0725.

^{1}H-NMR (NMR-16): δ2.44(s, 3H), 6.21(d, J=0.6Hz, 1H), 7.43-7.60(m, 3H), 7.89-7.93(m, 2H).

2-Benzoyl-4-deuteriofuran (51)

A mixture of 2-benzoyl-4-trimethylsilylfuran (**37**) (27mg, 0.1mmol) in chloroform (1mL) and deuteriated trifluoroacetic acid (1mL) was refluxed under N_2 for 6 days . Evaporation and chromatography (silica gel, EtOAc-hexanes 1:6) gave 2-benzoyl-4-deuteriofuran (**51**) as yellow liquid (18mg, 94%).

Mass spectrum: *m/e* 173 (M^+)

Exact mass: Calcd for $C_{11}H_7DO_2$, 173.0587; Found; 173.0586.

^{1}H-NMR (NMR-17, 19): δ7.24(s, 1H), 7.47-7.63(m, 3H), 7.72(s, 1H), 7.95-8.00(m,2H).

2-Benzoyl-3-deuteriofuran (52)

A mixture of 2-benzoyl-3-trimethylsilylfuran (**36**) (42mg, 0.2mmol) in chloroform (1mL) and deuteriated trifluoroacetic acid (1mL) was boiled under refluxed under N_2 for 4 days. Evaporation and preparative TLC (EtOAc-hexanes 1:6) gave 2-benzoyl-3-deuteriofuran (**52**) as yellow liquid (9mg, 100%) and unreacted 2-benzoyl-3-trimethylsilylfuran (**36**) (30mg).

Mass spectrum: *m/e* 173 (M^+)

Exact mass: Calcd for $C_{11}H_7DO_2$, 173.0587; Found: 173.0587.

^{1}H-NMR (NMR-18, 19): δ6.60(d, J=1.8Hz, 1H), 7.47-7.63(m, 3H), 7.72(s, 1H), 7.95-8.00(m, 2H).

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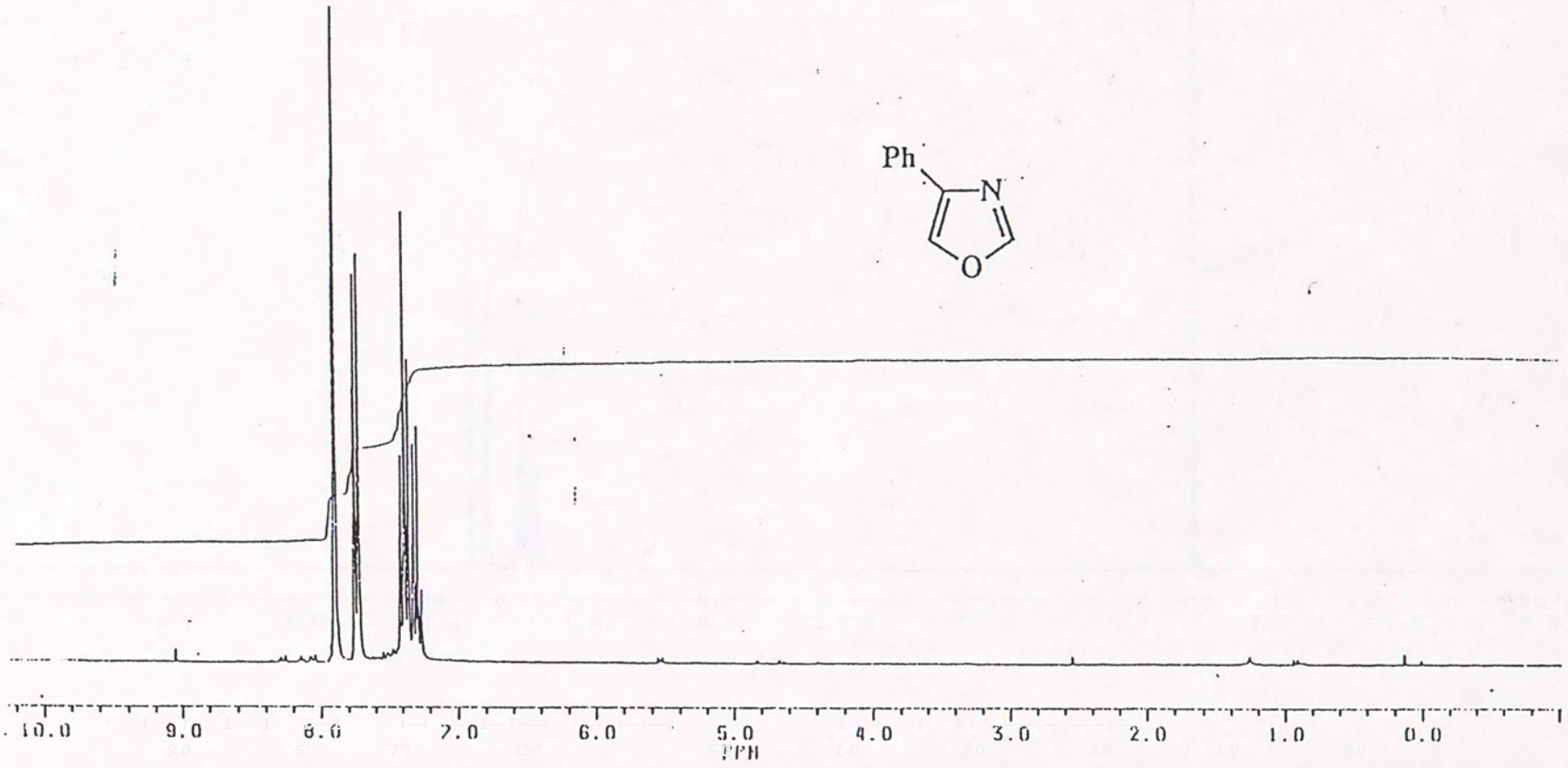
VIII. NMR Spectra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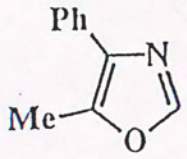
0.0
PPM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N
Me
O

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1.0
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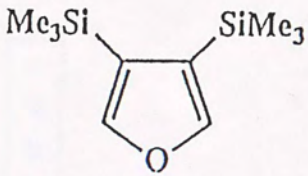
PPM



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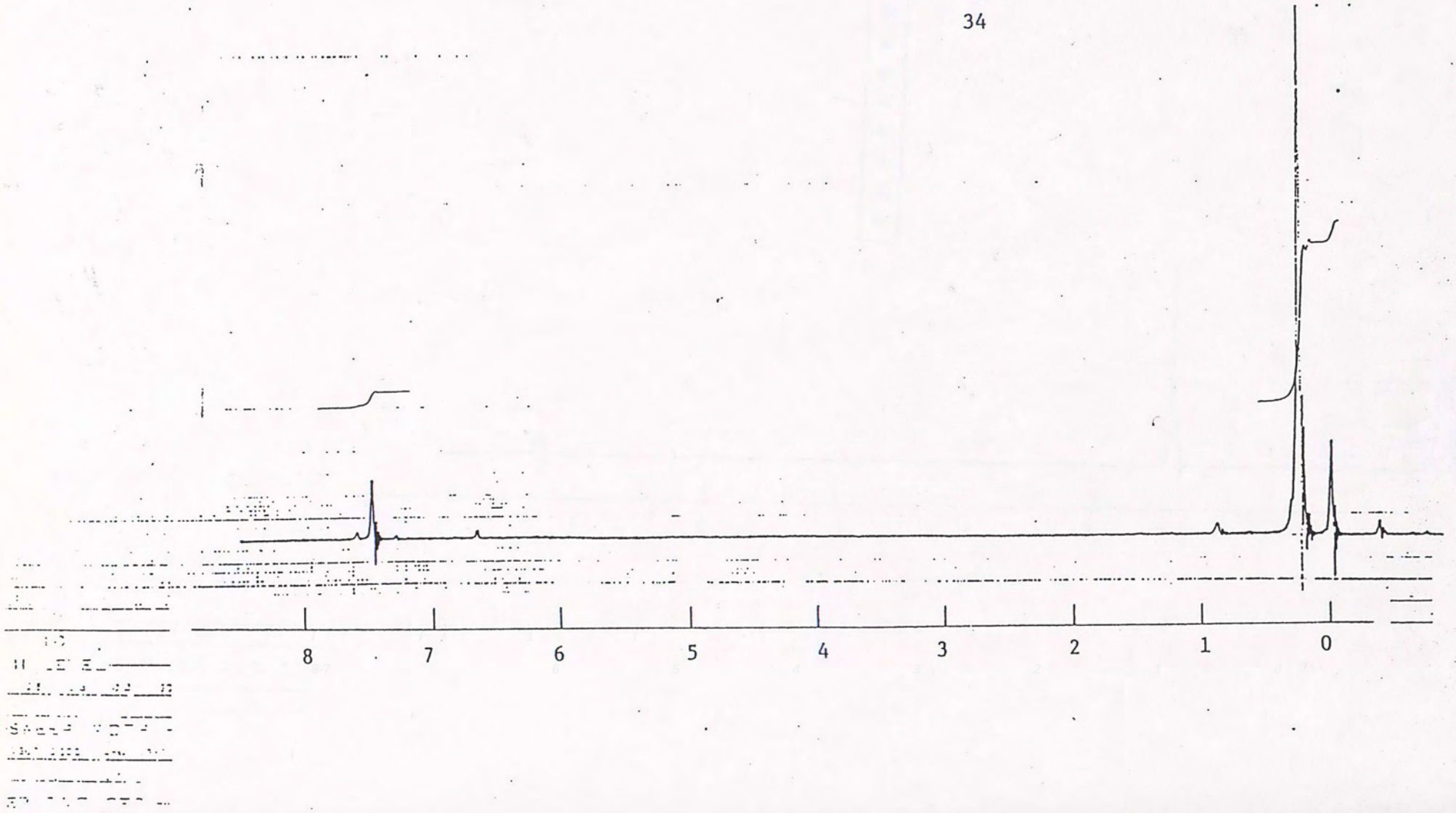

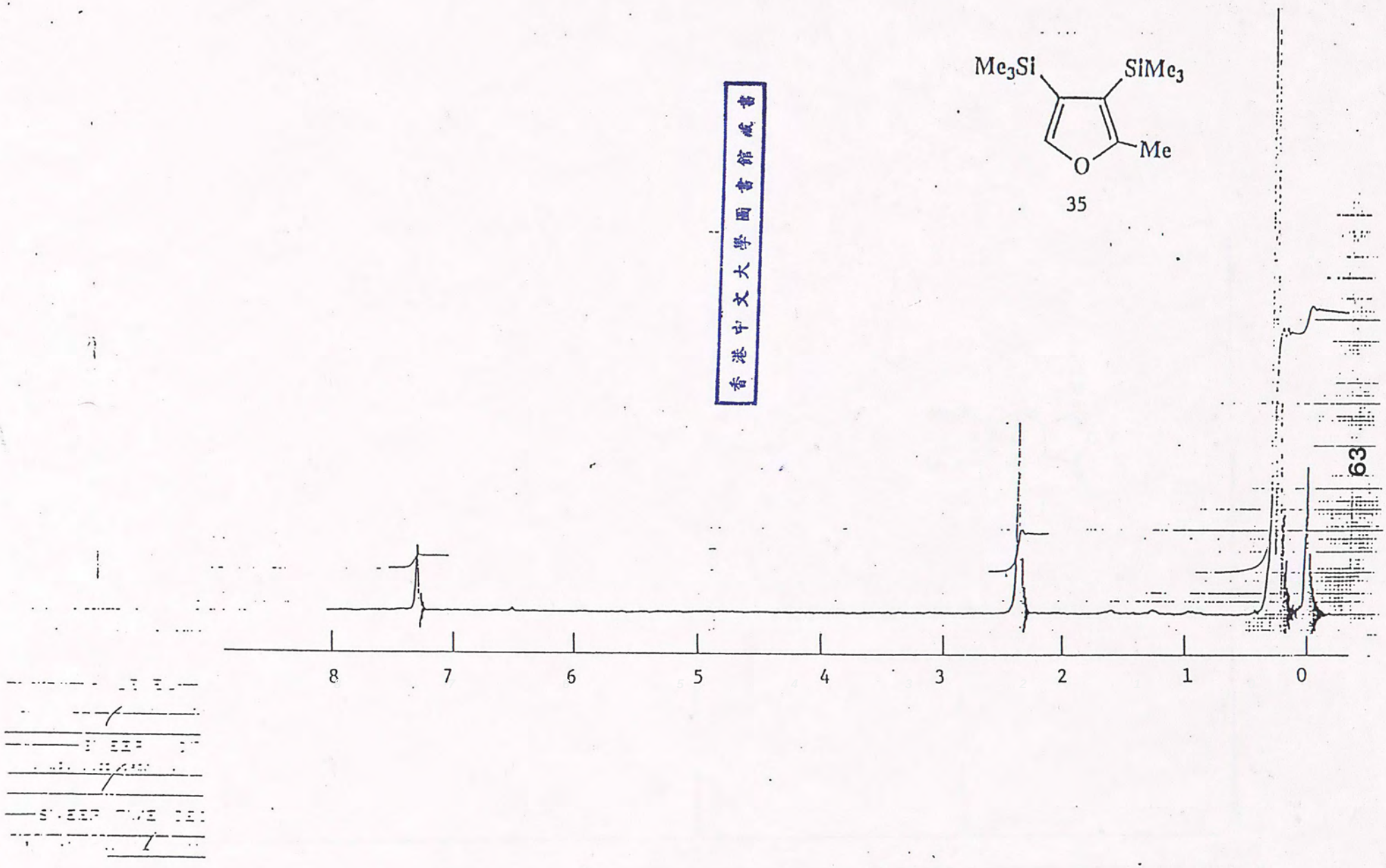

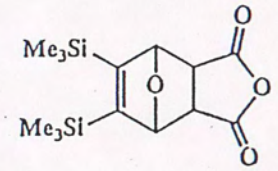

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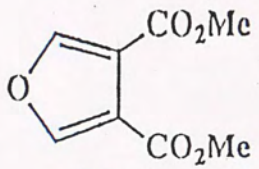

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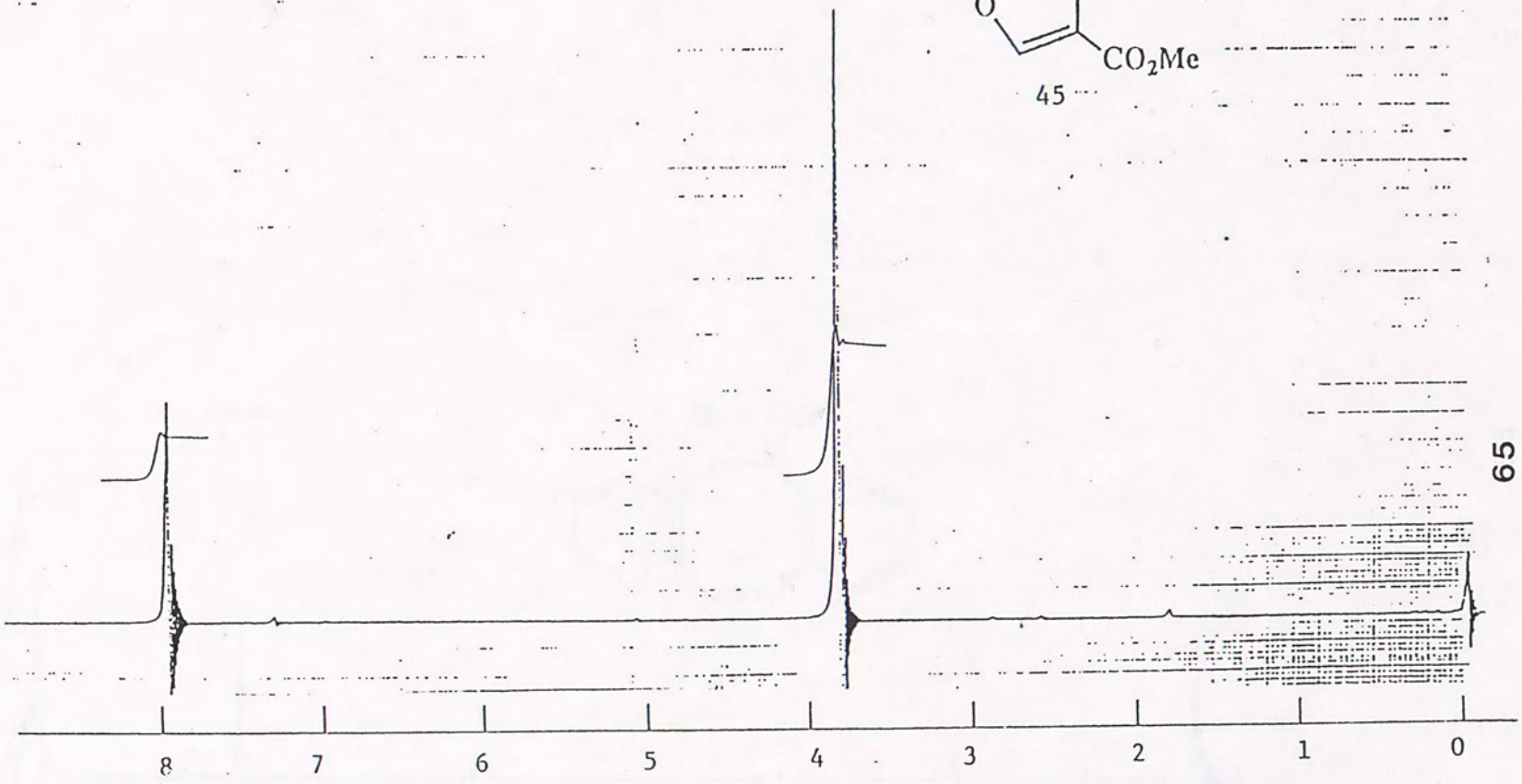

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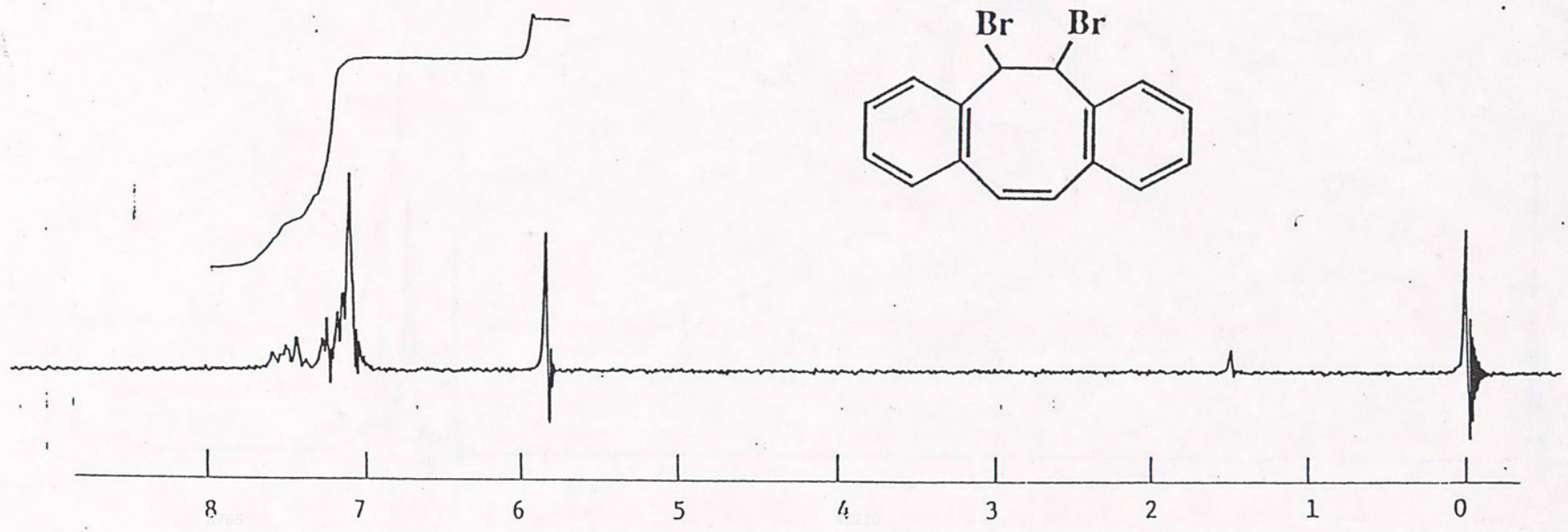
H LEVEL

SWEEP WIDTH

SWEEP TIME SEC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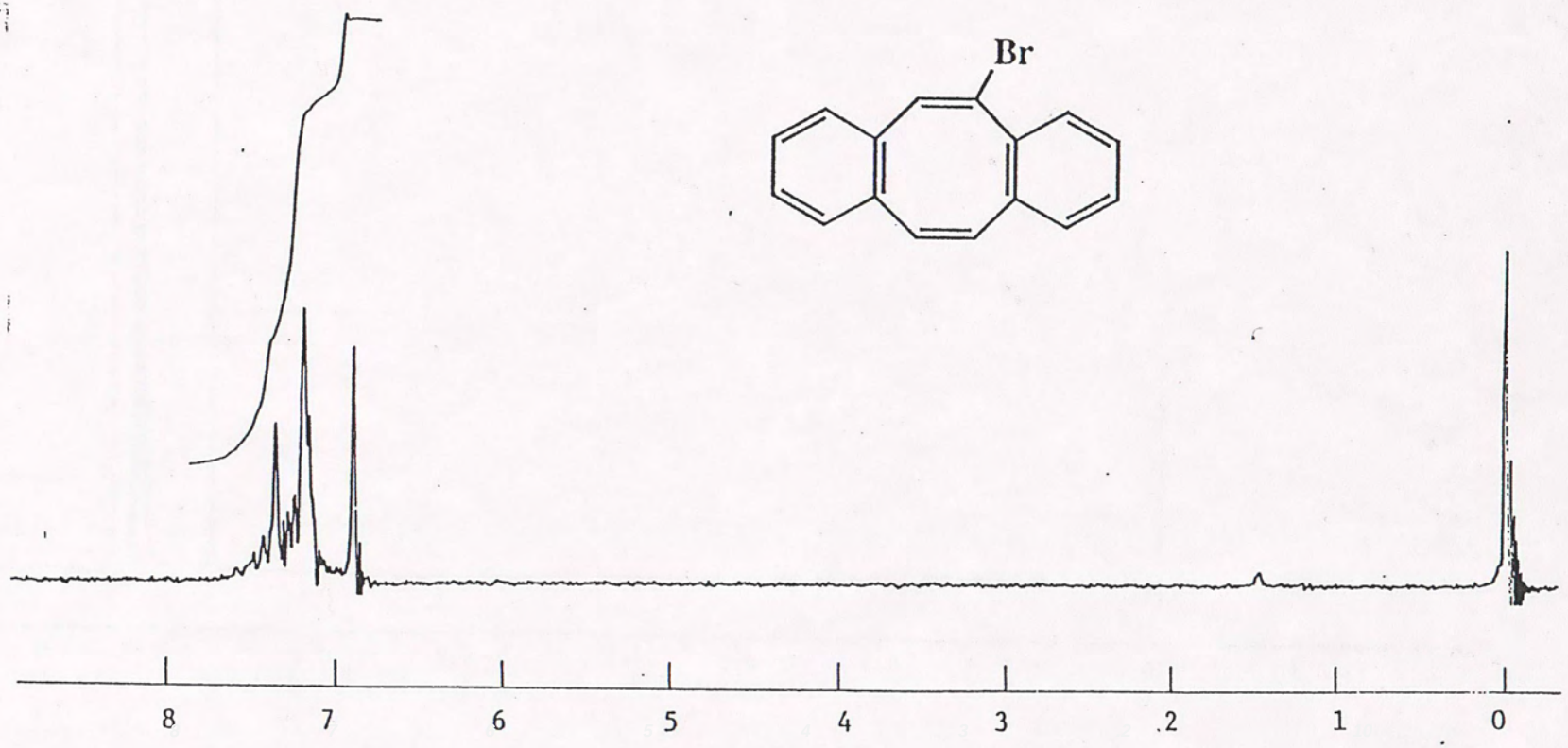
4
3
2
1
0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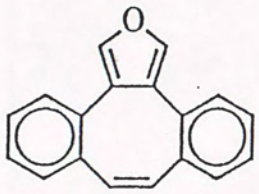

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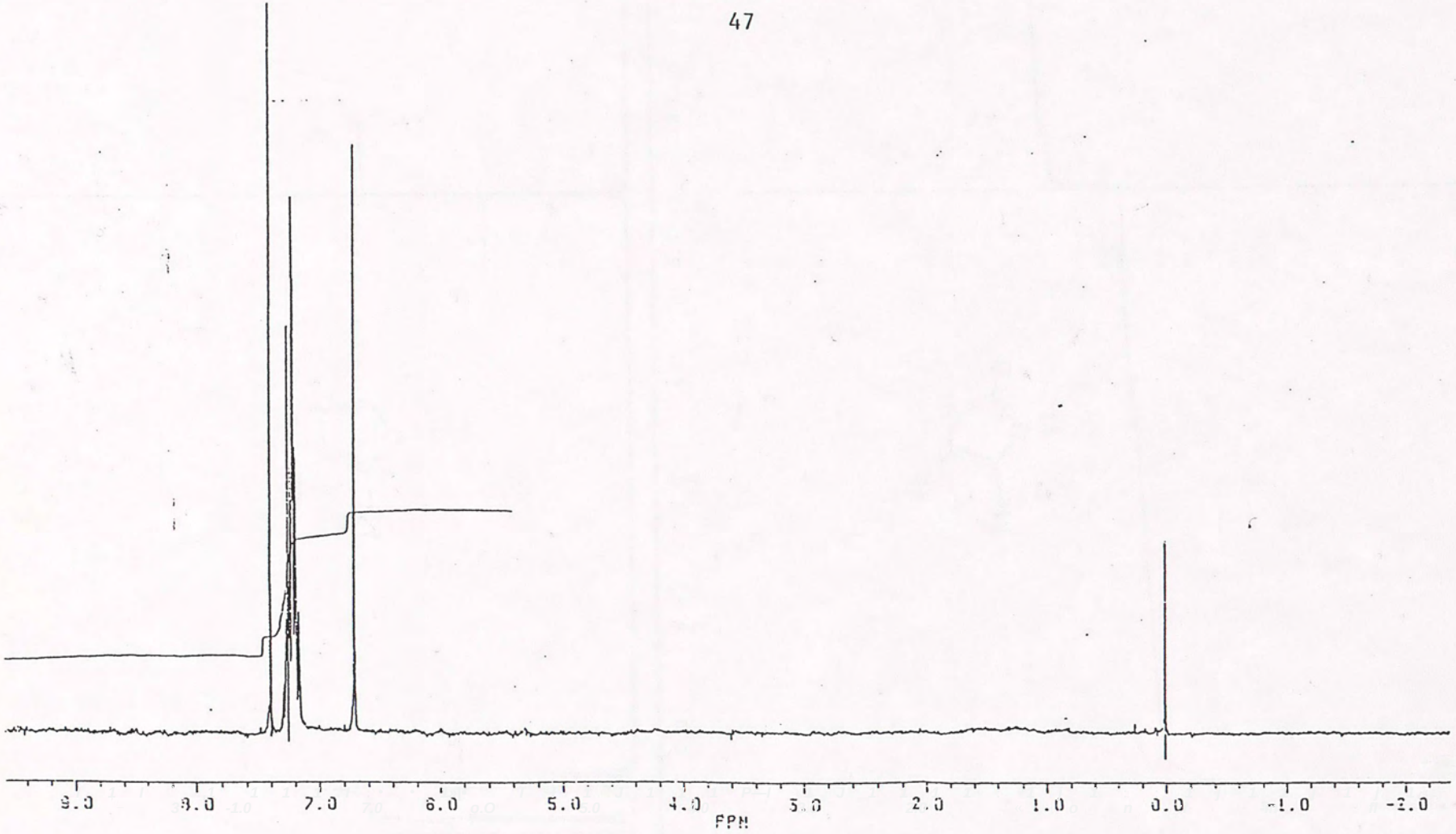

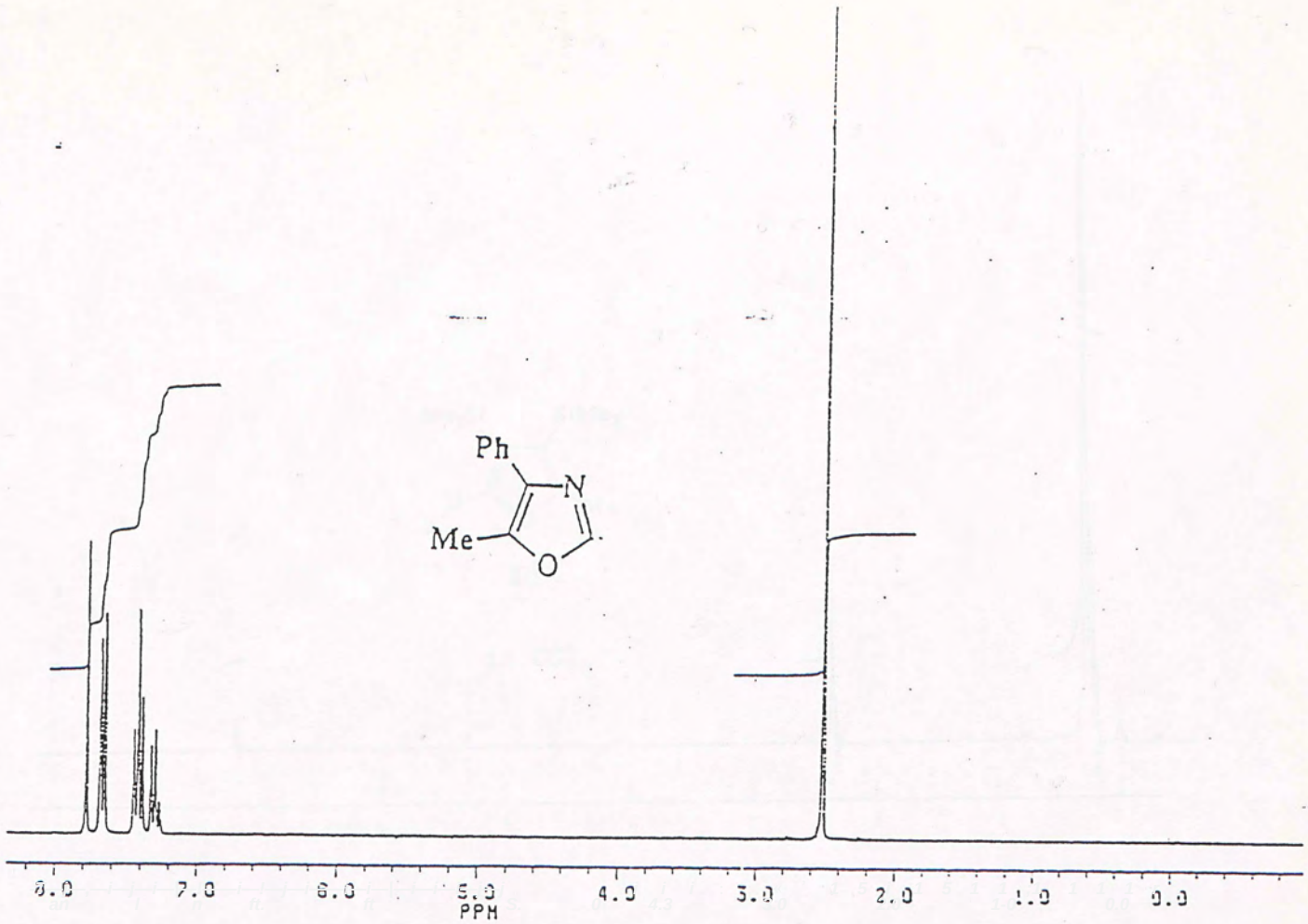
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Me
O
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PPM
4.0
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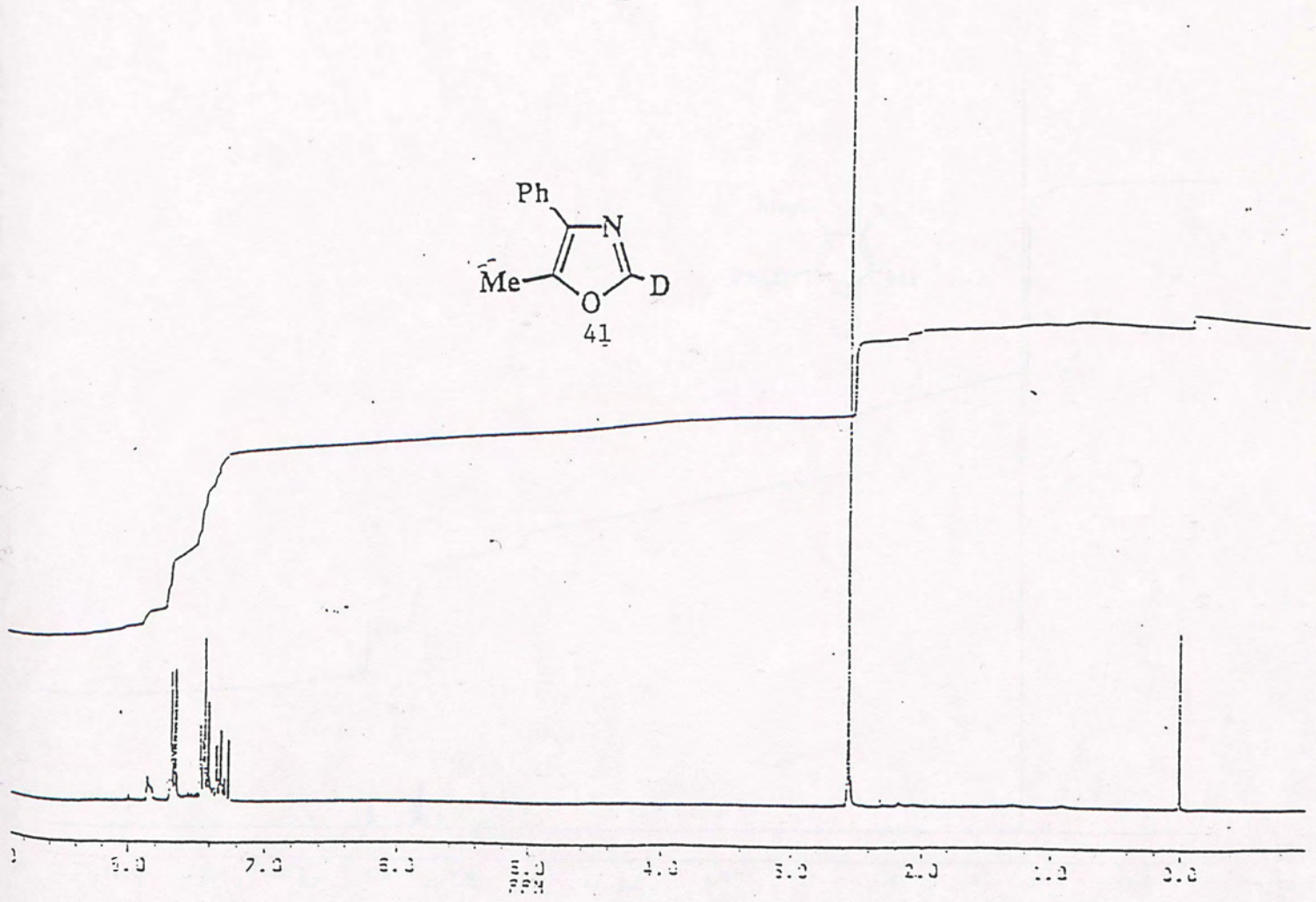
2.0
1.0
0.0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Me
O
D
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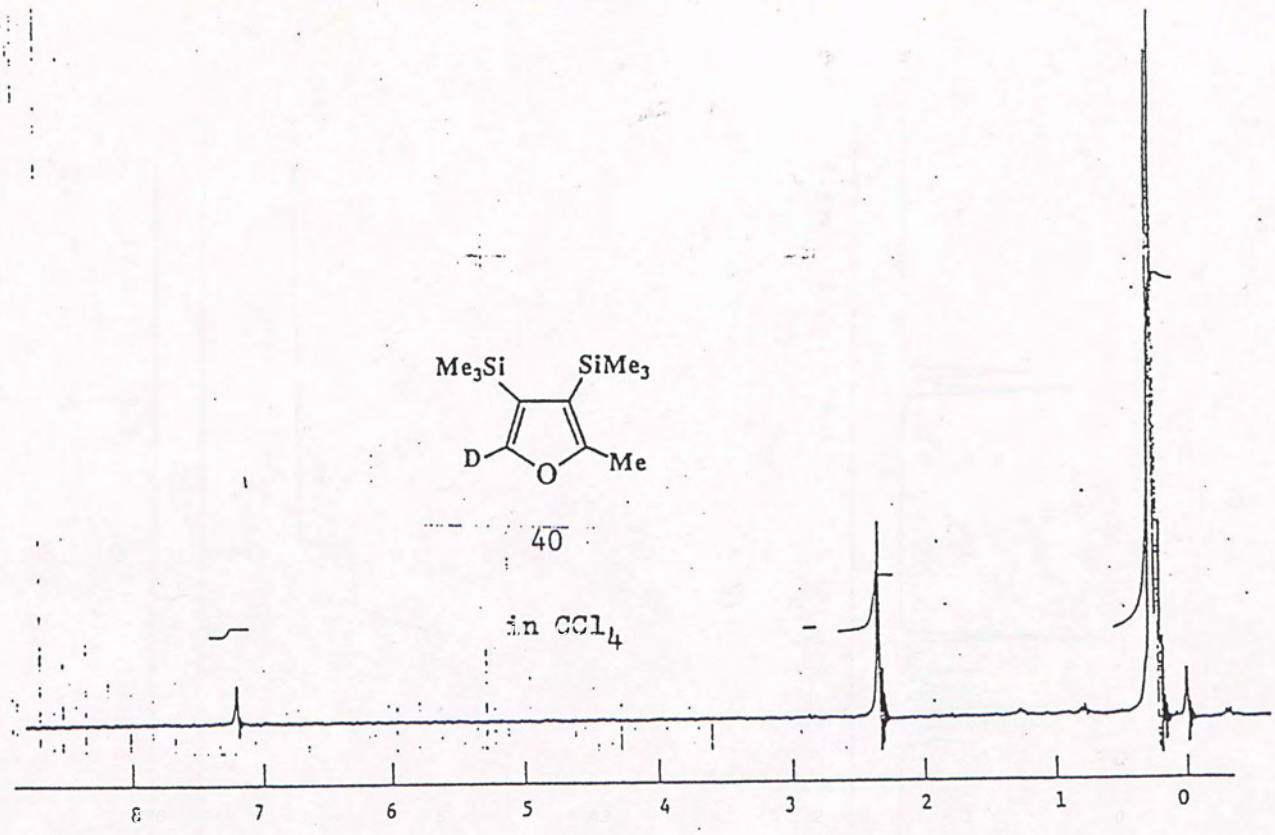
5.0
PPM
4.0
3.0
2.0

NMR-10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D
O
Me
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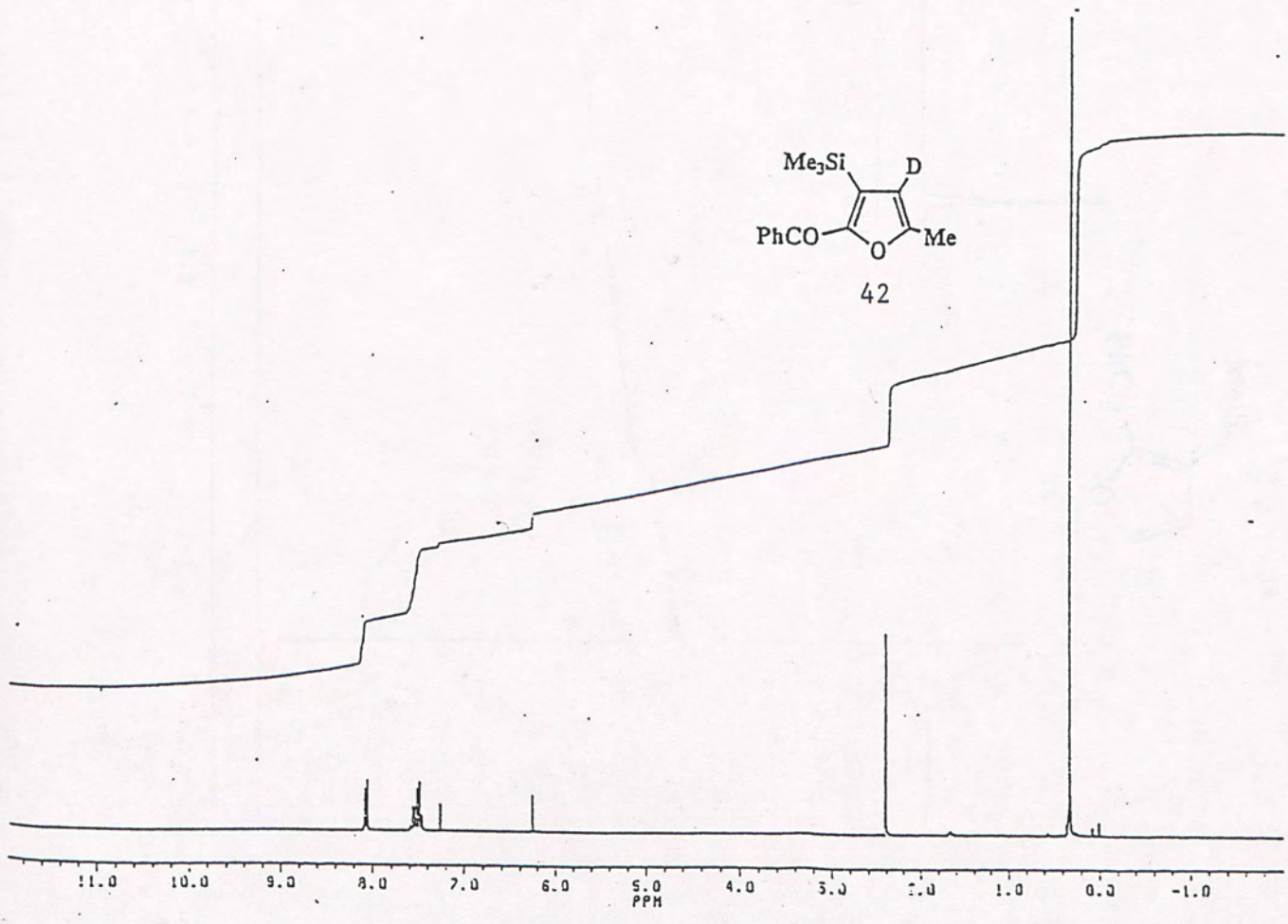
in CCl4
8
7
6
5
4
3
2
1
0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D
PhCO
O
Me
42
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10.0
9.0
8.0
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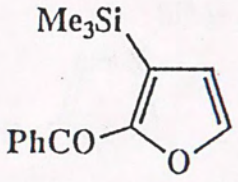
6.0
5.0
PPM
4.0
3.0
2.0
1.0
0.0
-1.0

NMR-11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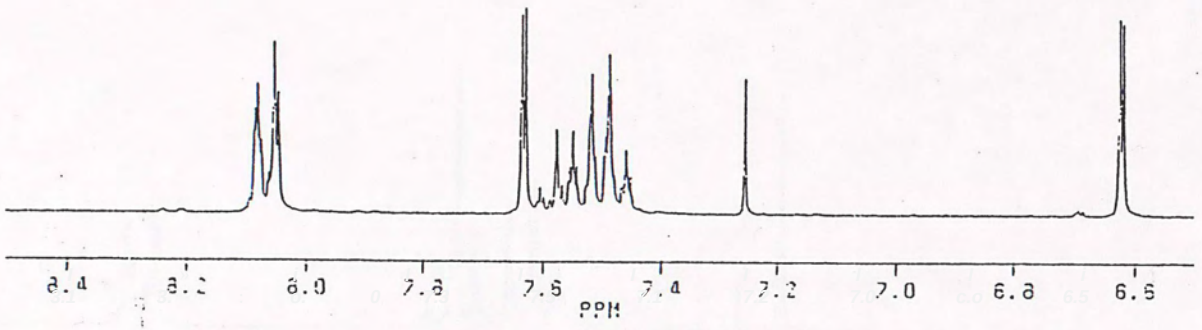
PhCO
O

36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7.6
7.4
7.2
7.0
6.8
6.6
PPM

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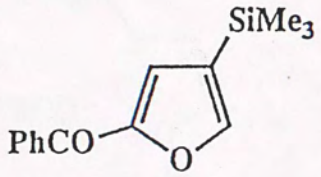
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM



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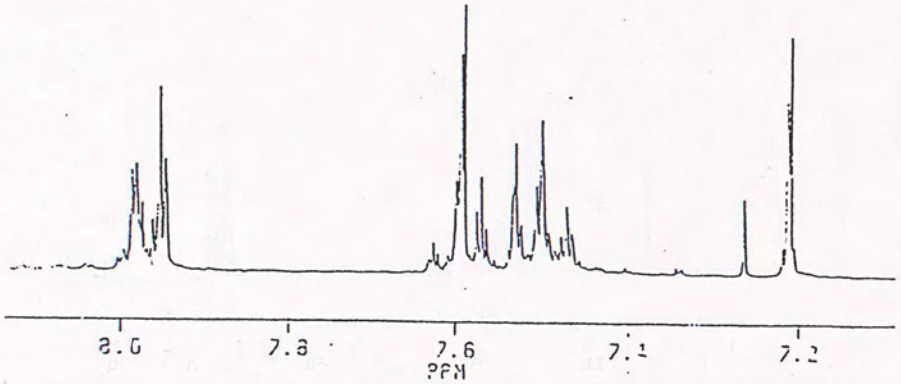

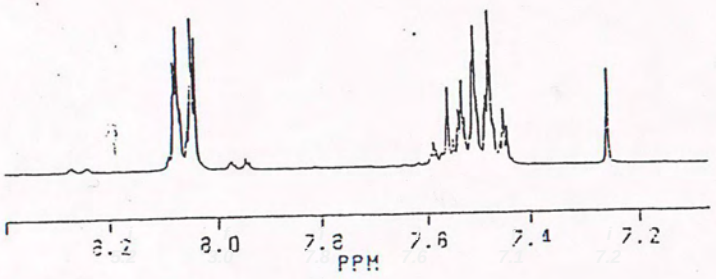
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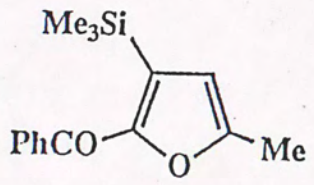
7.8
7.6
7.4
7.2
PPM


Me3Si
PhCO
O
Me

38

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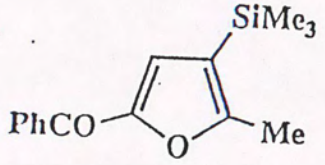
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM



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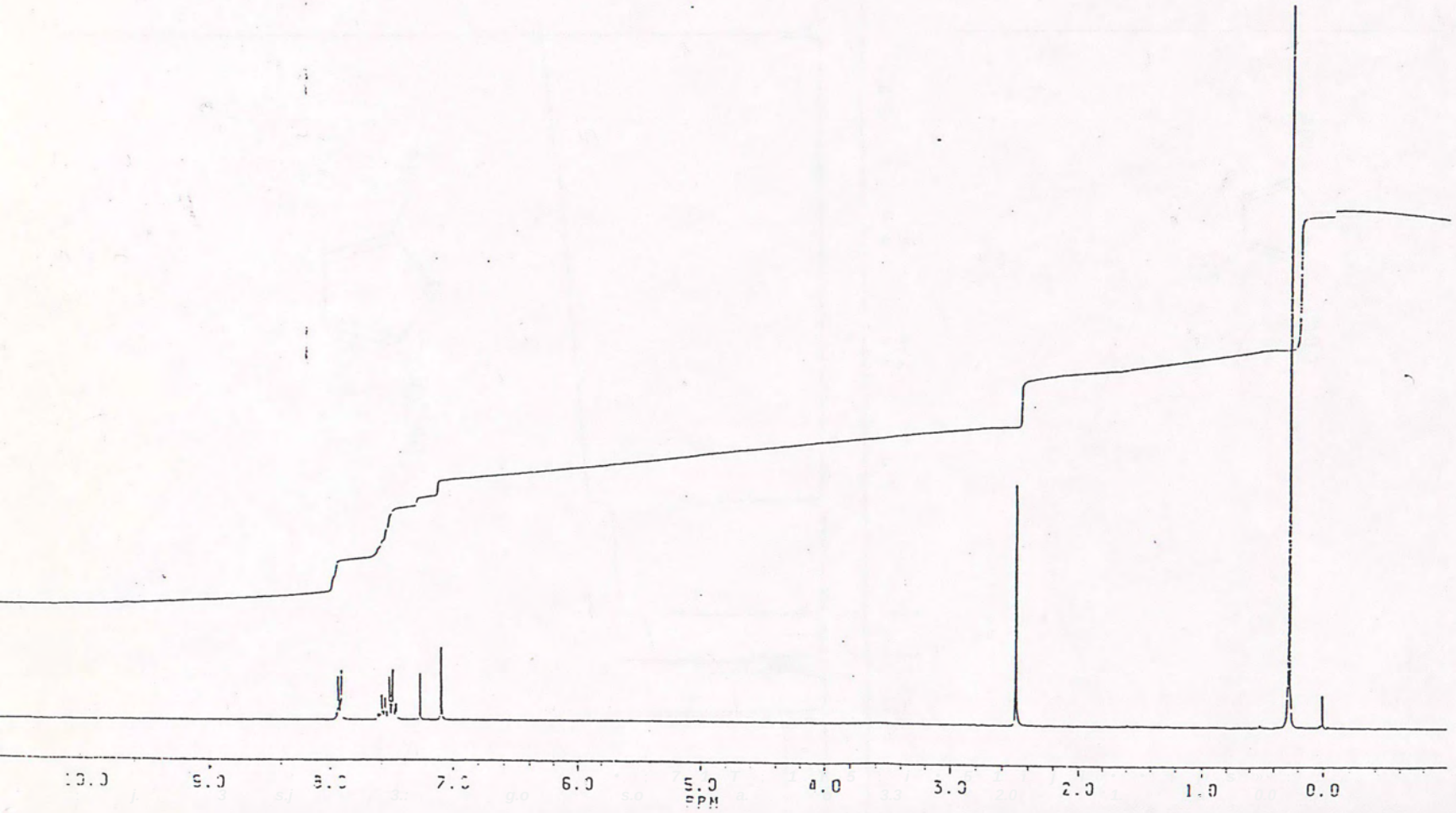

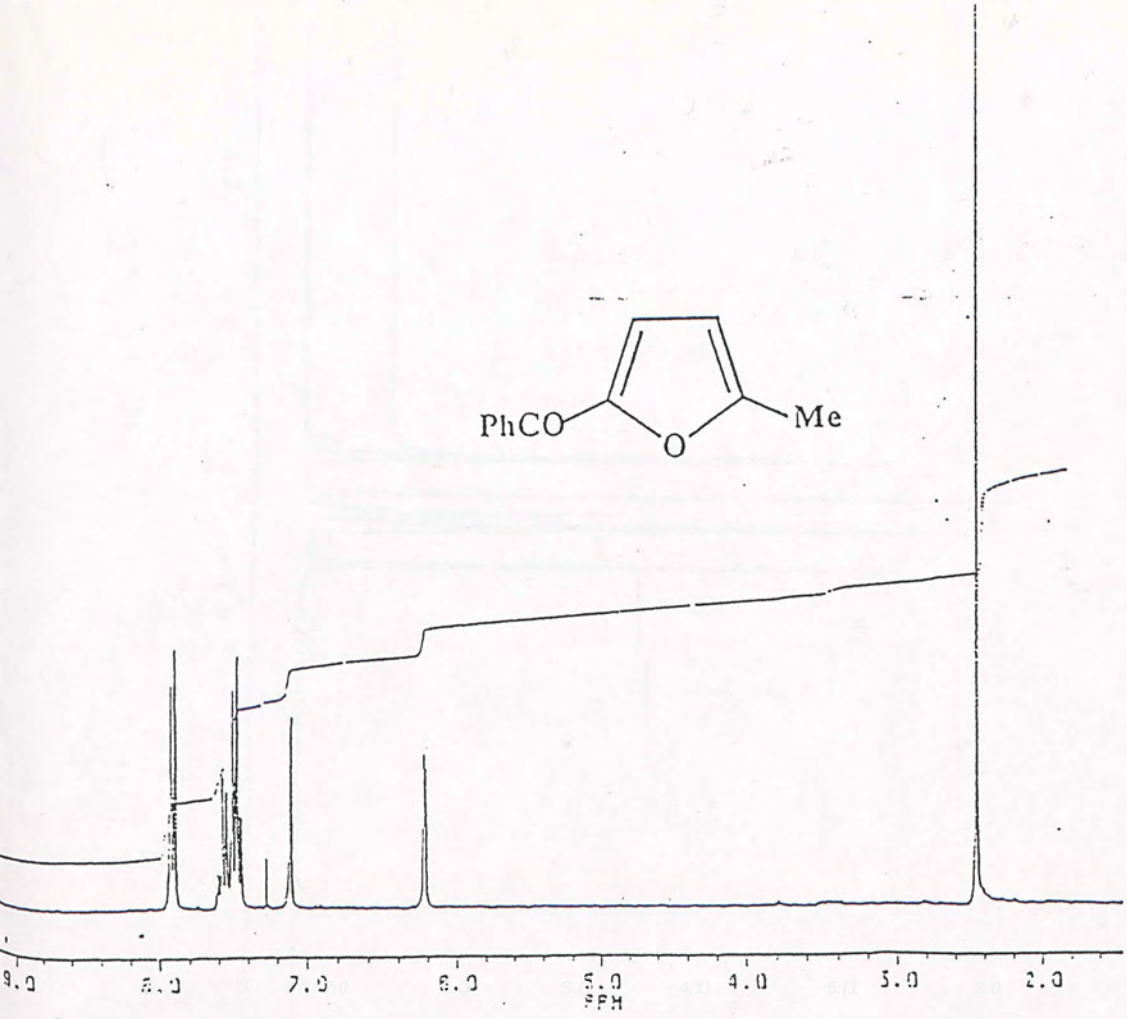

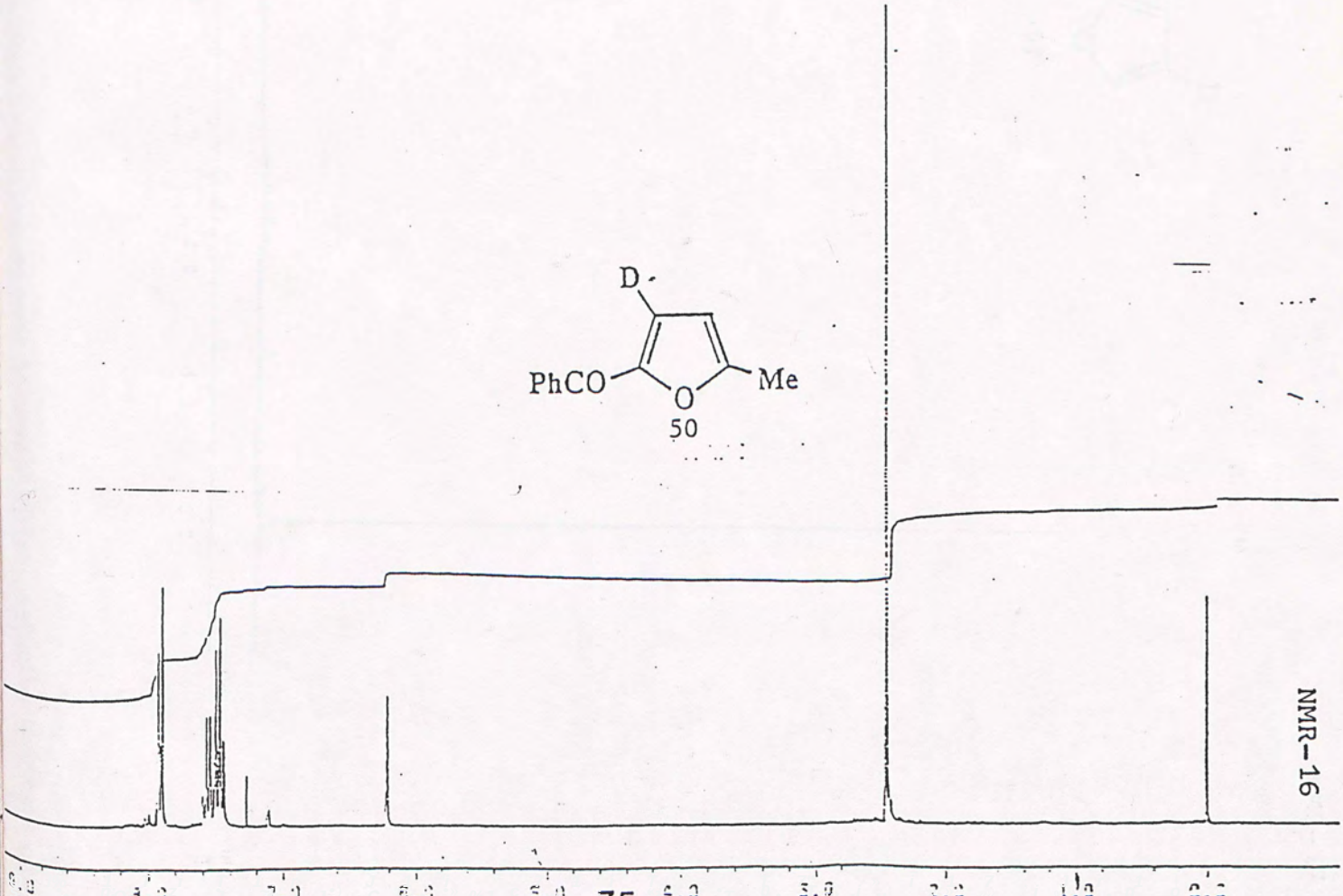

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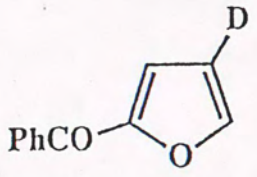

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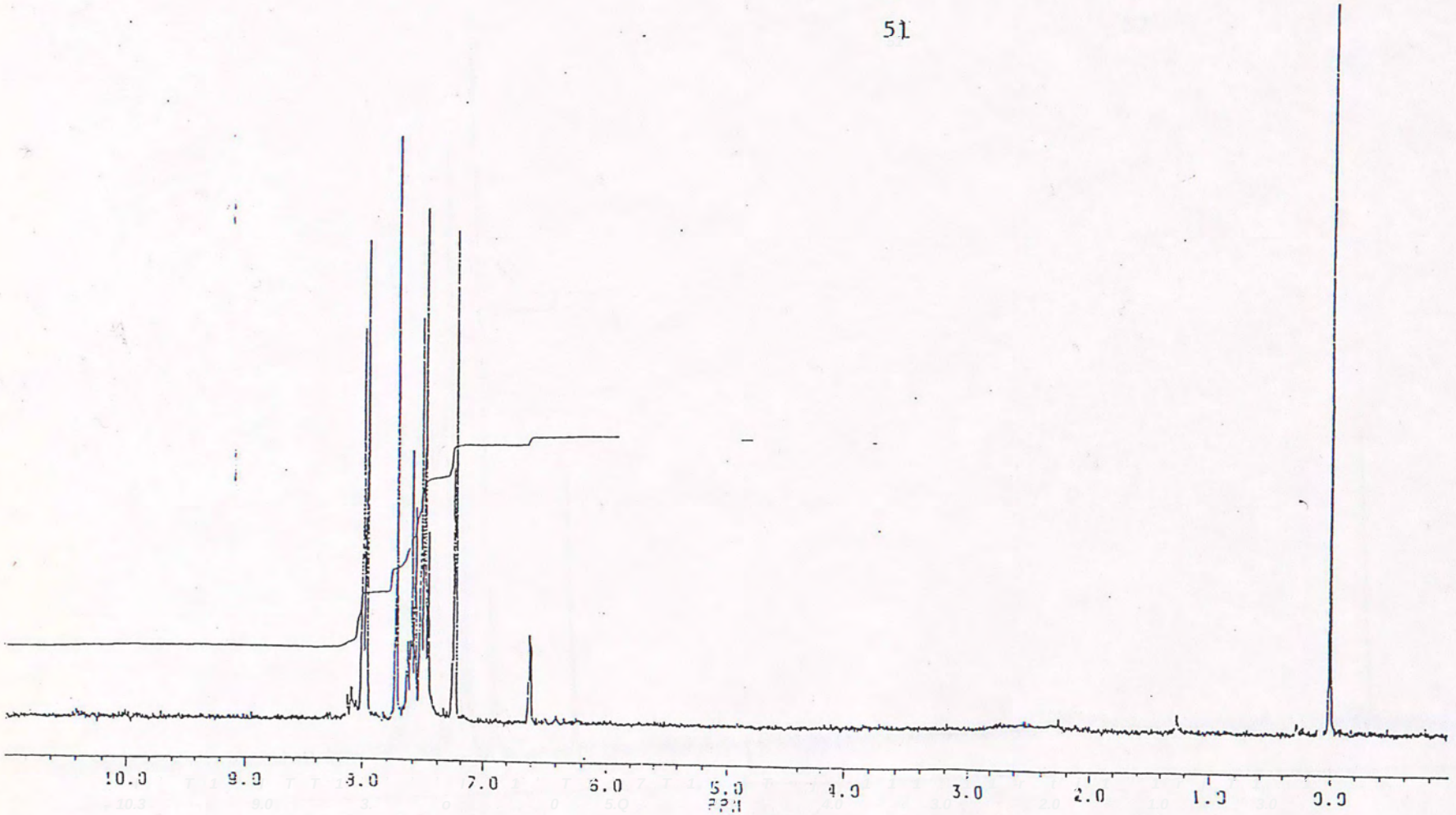

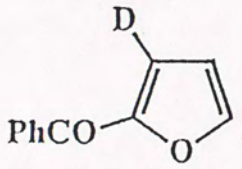

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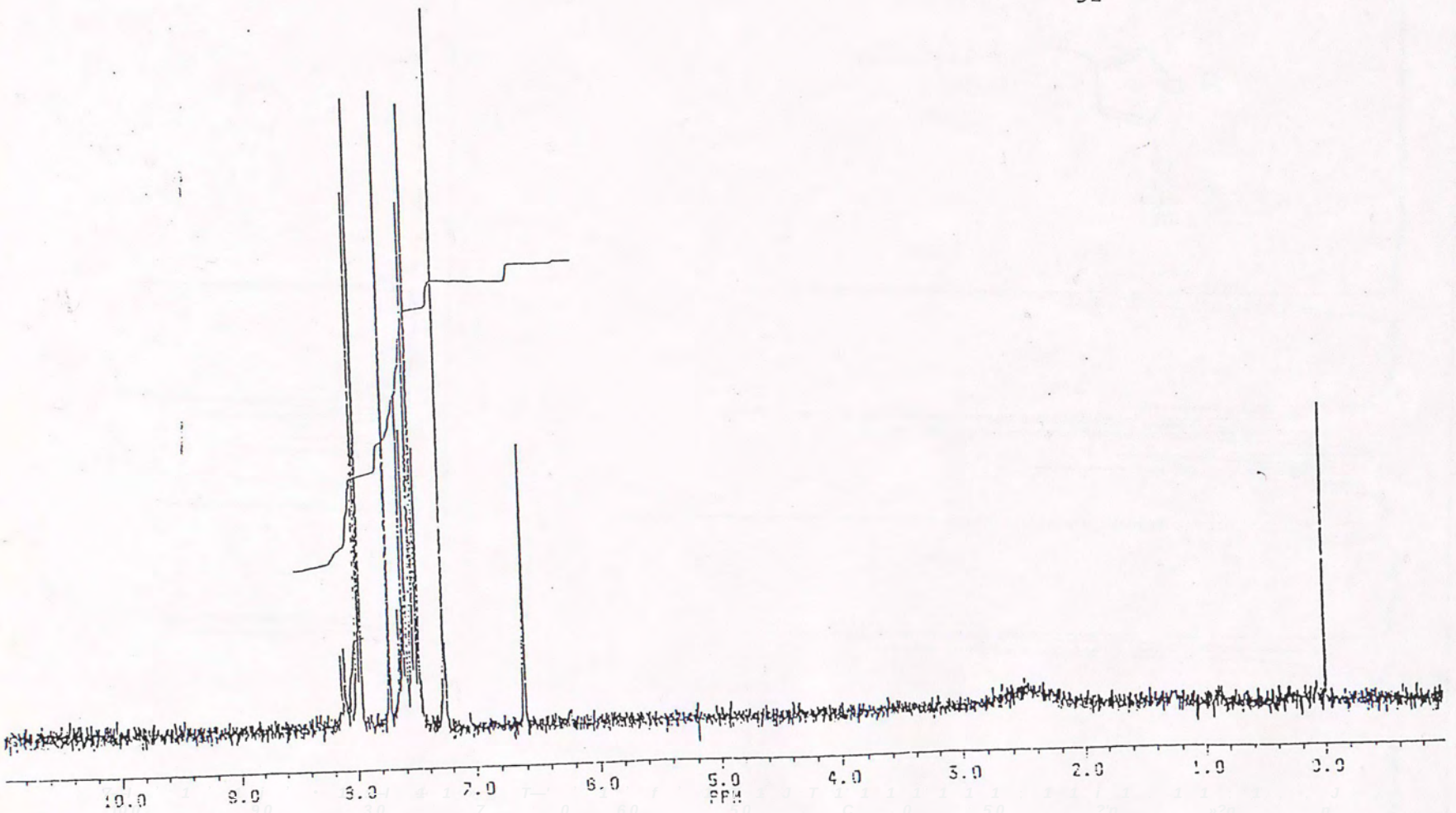

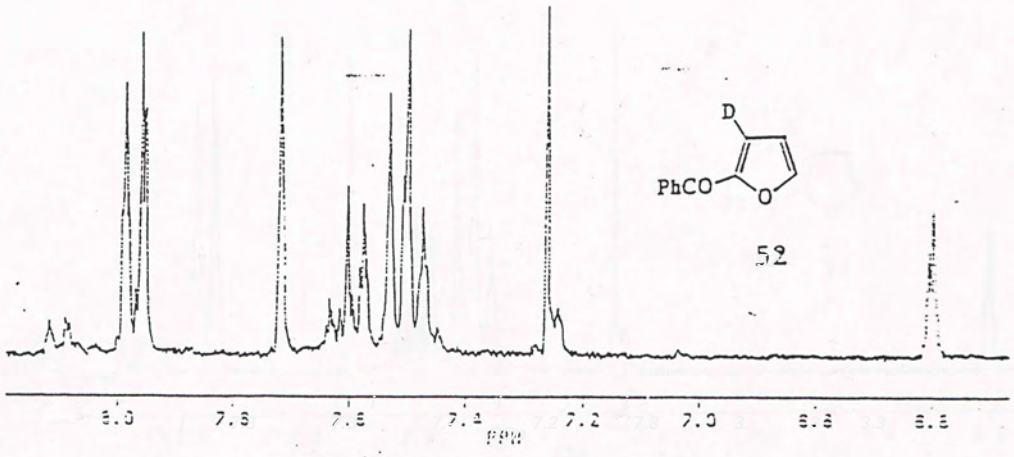
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O
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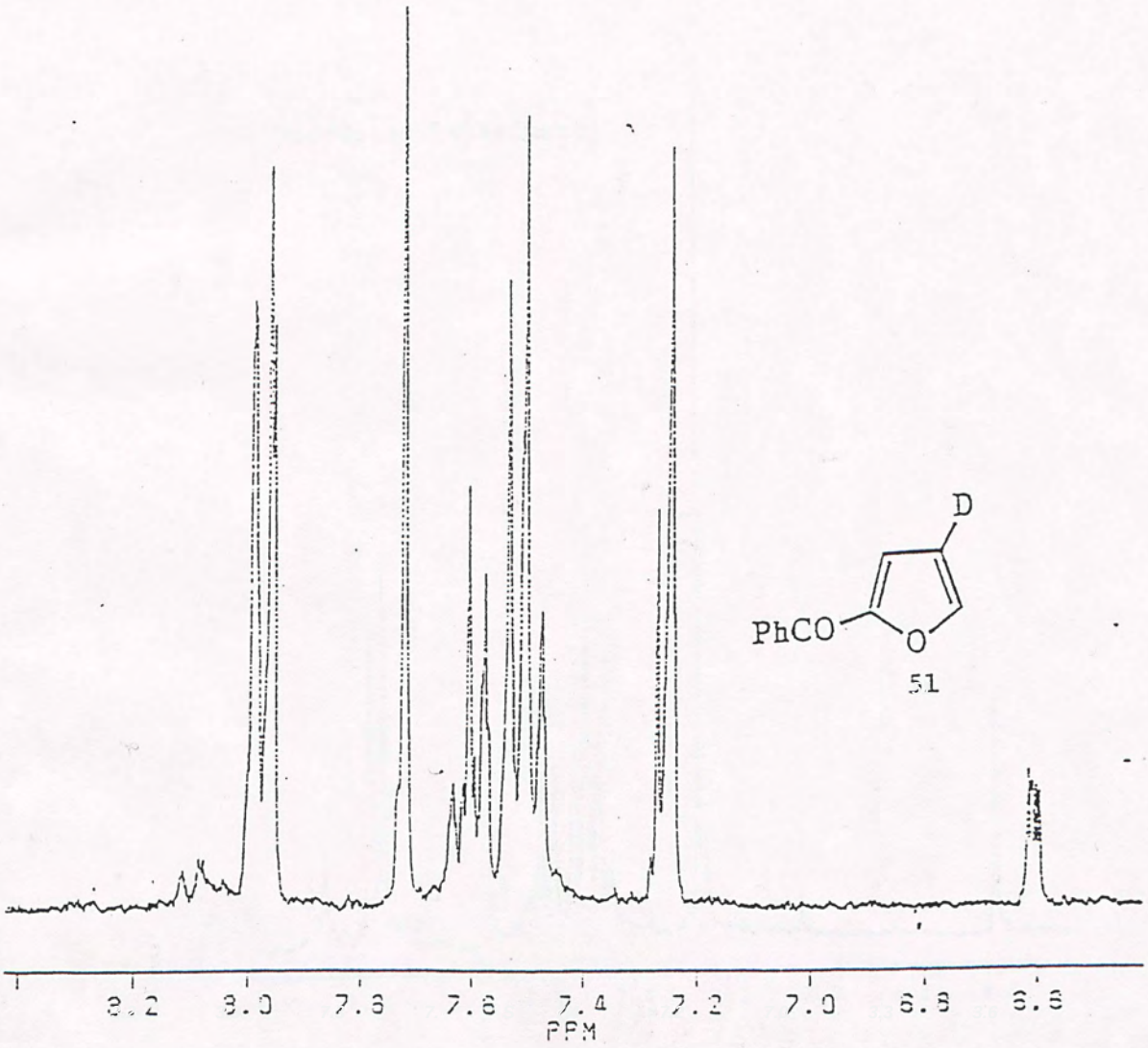
7.4
7.2
7.0
6.8
6.6
PPM

52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PhCO
O
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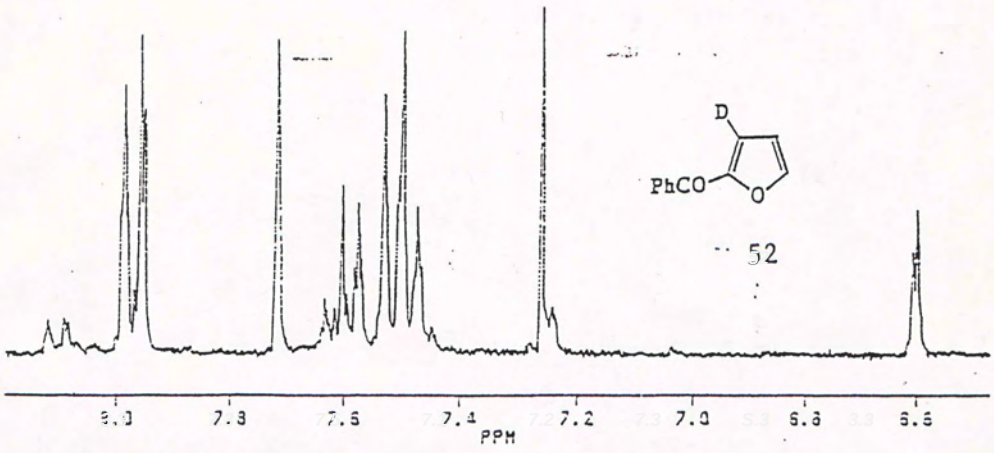
6.8
6.6
PPM

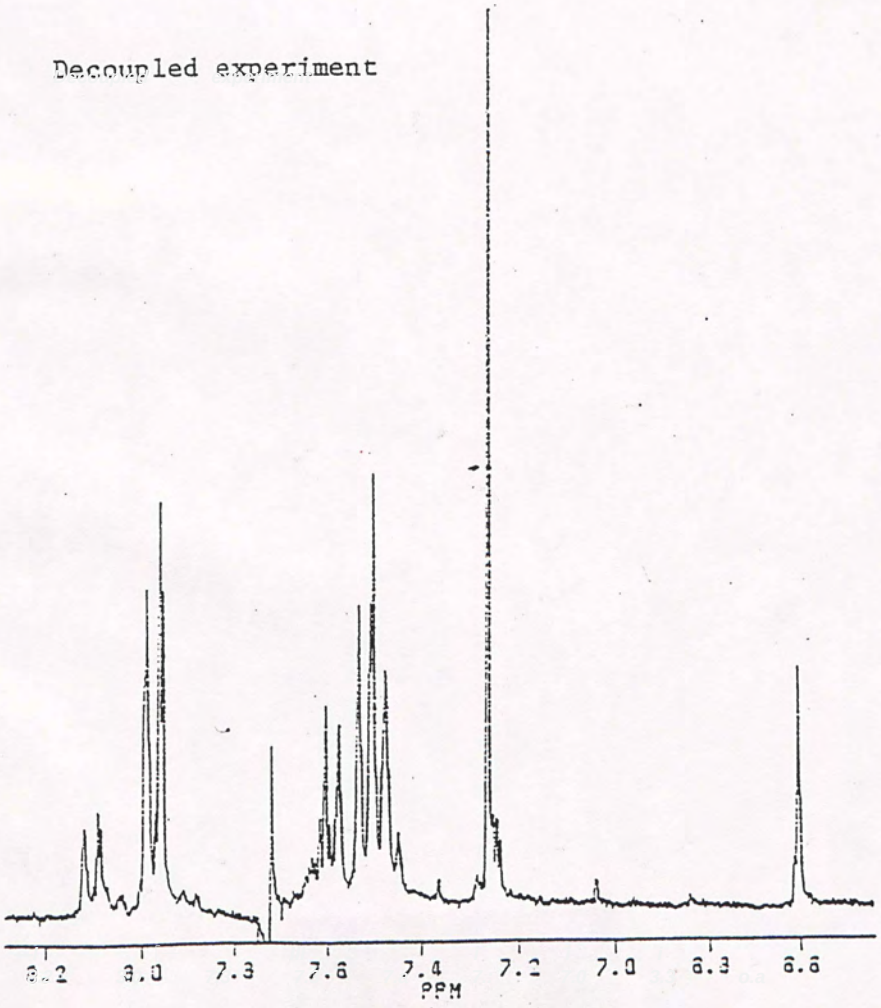
51

NMR-19



52

Decoupled experiment



NMR-20